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UNEXPECTED DEATH IN INFANTS AND YOUNG CHILDREN: SECOND SERIES.

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In a former study of deaths in infancy one of us strongly favoured the view that babies alleged to have suffocated accidentally in bed had probably died from undiscovered natural disease. Furthermore, the stand was taken that the more thorough the autopsy, the less the likelihood of a diagnosis of "accidental suffocation". It was demonstrated that, in the absence of any gross pathological findings *post mortem*, histopathological studies showed that many of these infants were suffering from acute infections of various types (Bowden, 1950).

To elucidate further this question of unexpected death in infants we have endeavoured: (i) to show that the syndrome "sudden death in infants" is epidemiologically related to evidence of infections of one kind or another in the community concerned; (ii) to accumulate histopathological data in a further consecutive series of cases of "sudden death" in infants, at the same time gathering evidence that the findings regarded as significant in these cases were not present in children of similar age who died a violent death during the same period; (iii) to determine by bacteriological examination whether death was due to or associated with bacteriæmia of recognized pathogens; (iv) to seek for evidence that on occasions influenza virus, the only respiratory virus available for laboratory study, may be the responsible pathogen.

The present study sets out the post-mortem findings in 43 children who died suddenly. Many were found dead in bed, and their bodies were brought to the Melbourne City Morgue for examination. In 22 of them complete bacteriological examination was carried out, in addition to attempts to isolate influenza virus from lungs and trachea. The results obtained provide further considerable support for the previously expressed view that accidental mechanical suffocation of infants by bedclothes is a rare occurrence.

POST-MORTEM FINDINGS AND CLINICAL HISTORIES.

Abbreviated accounts of the significant autopsy findings and of any relevant histories that were obtainable are set out in Table I. It was often difficult to obtain an accurate account of the child's condition in the period immediately preceding his unexpected death. The information most frequently proffered at first was that the child was quite well when last seen. However, if the parents were interviewed some time later, when the emotional intensity of the experience had faded somewhat, it was often possible to elicit by careful questioning a history of preceding ill health in the child. In 29 of these 43 children a carefully taken history revealed evidence of several days or weeks of minor ill health.

Bacteriological Findings and their Significance.

Technique.

The technique employed was as follows.

A set of dissecting instruments sterilized by autoclaving was taken to the post-mortem room. In addition, sterile containers and throat swabs were provided.

[1] Work done with the aid of a grant from the National Health and Medical Research Council, Australia.

TABLE I.

Case Number.	Child's Sex and Age.	How Found.	Macroscopic Findings.	Microscopic Findings.	Bacteriological Examination.	History.
1	F. 5 weeks.	Dead in perambulator.	Fallot's tetralogy.	Nil.	Not made.	Known to have had congenital heart disease.
2	M. 4 weeks.	Dead in cot.	No definite abnormality.	Acute bronchitis and bronchiolitis, pulmonary œdema.	Not made.	Nil.
3	F. 6 months.	Dead face down in pillow.	Mucosa of trachea and bronchi reddened, congested meninges.	Acute myocarditis, acute bronchitis.	Not made.	Suffering from heavy cold. Usual sleeping position over on face.
4	M. 41 hours.	Died whilst being transferred from one hospital to another.	Hæmorrhage from ruptured vein of Galen, bilateral suprarenal hæmorrhages.	Partial atelectasis of lungs.	Not made.	Baby seven weeks premature.
5	M. 3 months.	Dead face down in pillow.	No abnormality detected.	Pulmonary œdema and focal collections of polymorphonuclear leucocytes in liver and lung.	Not made.	Crying and restless during night.
6	M. 9 months.	Dead in bed.	Thin purulent otitis, reddened larynx, trachea and bronchi.	Laryngo-tracheo-bronchitis.	Not made.	Treated for 24 hours by doctor for gastro-enteritis.
7	F. 13 months.	Comatose when examined by doctor.	Petechial blotchy rash on skin, œdema about suprarenals, reddened larynx, trachea and bronchi.	Acute tracheo-bronchitis, early meningitis.	Not made.	Had a cold for some days. Off food for 12 hours.
8	M. 19 months.	Dead in bed with mother.	Blotchy, macular rash on body, acute hæmorrhagic pericarditis, acute right-sided pleurisy.	Acute pericarditis, acute pleurisy, acute bronchitis.	Growth of *Neisseria meningitidis* from pericardial fluid.	Was restless and appeared ill for 24 hours before death.
9	M. 3·5 months.	Dead face downwards.	Patchy hæmorrhages in lungs near hilus.	Acute bronchitis.	Staphylococcus coagulase-positive cultured from nose and trachea.	Treated by doctor that day.
10	F. 5 months.	Found dead in cot.	Blotchy rash on lower extremities, semi-purulent material in each ear.	Acute bronchitis, early meningitis.	No significant findings.	Apparently well.
11	M. 1 month.	Dead in cot.	Hæmorrhages on lungs.	Acute bronchitis and bronchiolitis.	No significant findings.	Cough and running nose for one week.
12	M. 5 months.	Dead face downwards in perambulator.	Right *otitis media*.	Acute tracheitis and bronchitis.	Staphylococcus coagulase-positive in nose and trachea.	Had a cold for three days.
13	M. 4·5 months.	Died in perambulator face down on pillow.	Left *otitis media*, petechiæ on heart and lungs.	Nothing definite.	Heavy growth in pure culture of pneumococcus from left middle ear and heart blood.	Apparently well.
14	M. 2·5 years.	Found dead in bed.	Nil.	Acute trachec-bronchitis.	Not made.	Apparently well. Blind since birth.
15	M. 4 weeks.	Dead in cot.	Increased pericardial fluid, straw-coloured fluid in peritoneal cavity and advanced thrush in mouth and œsophagus.	Acute pyelonephritis.	Heavy growth of *Escherichia coli* obtained from heart blood, spleen, pericardial fluid, brain, lung, trachea and nose.	Treated for thrush. Vomiting before death, less than 24 hours' duration.
16	M. 19 months.	Dead in bed.	Blotchy purplish rash on skin.	Acute tracheo-bronchitis.	No significant findings.	Drowsy two hours before death.
17	M. 11 weeks.	Found dead in bed.	No definite abnormality.	Acute bronchopneumonia.	No significant findings.	Restless, irritable and vomiting after food for three days before death.
18	F. 3 months.	Dead in bassinette.	Underweight (seven pounds), petechiæ on heart, lungs and thymus.	Acute tracheo-bronchitis.	No significant findings.	Apparently well.
19	M. 5 months.	Dead in cot.	Petechiæ on heart, lungs and thymus.	Early meningitis.	A few hæmolytic streptococci Group A in cultures from the lungs and trachea.	Five weeks premature, appeared well night before death, found dead at 6.30 a.m.
20	M. 4 months.	Dead face downwards in cot.	Nil.	Acute bronchitis.	No significant findings.	Fed and changed in afternoon, appeared well, found dead at 6.45 p.m.
21	M. 10 months.	Found face down.	Obvious lividity, petechiæ on surface of heart, thin mucopus in right ear.	Tracheo-bronchitis.	No significant findings.	Had a running nose, was suffering from a respiratory infection, two other children also ill.
22	M. 6 months.	Died on arrival at hospital.	Reddened trachea, mucopus in left ear.	Tracheo-bronchitis.	No significant findings.	Cough for three days, convulsions for five hours before death, temperature 103° F. Treated with penicillin and sulphonamide.
23	F. 7 weeks.	Dead in cot.	Cradle-cap.	Early meningitis.	Not made.	Thought to be well.

TABLE I.—*Continued.*

Case Number.	Child's Sex and Age.	How Found.	Macroscopic Findings.	Microscopic Findings.	Bacteriological Examination.	History.
24	M. 15 months.	Dead face downwards.	Right upper lobe bronchiectasis and bronchopneumonia. Underweight—12 pounds.	Fibrocystic disease of pancreas, bronchiectasis, bronchopneumonia.	Staphylococcus coagulase-positive cultured from nose, trachea, both ears, lung and liver.	Three attacks of bronchopneumonia since birth.
25	F. 5 months.	Dead when seen by doctor.	A few petechiæ on lungs.	Early meningitis.	Not made.	Screamed for 20 minutes before death.
26	F. 10 weeks.	Dead in cot.	Subpleural hæmorrhages, hæmorrhages on heart.	Inhalational pneumonia following aspiration of amniotic contents, hepatitis.	Not made.	Cried at 6 a.m., then went to sleep; found dead at 10 a.m.
27	M. 4 months.	Died on way to hospital.	Nil.	Patchy acute interstitial myocarditis, bronchitis.	Not made.	Off food on day of his death.
28	M. 11 months.	Died suddenly.	No definite abnormality.	Acute bronchitis.	Not made.	Suffering from a cold for six days, died suddenly.
29	M. 9 months.	Dead in bed.	Hæmorrhages on heart and lungs.	Early meningitis.	Staphylococcus coagulase-positive cultured from heart blood and spleen.	Several days' illness, treated for pneumonia, died suddenly.
30	F. 3 weeks.	Dead in bed with mother and another child.	Hæmorrhages on heart and lungs.	Acute bronchitis.	Not made.	Taken into bed because crying during night.
31	M. 6 months.	Dead in perambulator.	Reddened larynx and trachea, left *otitis media*.	Laryngo-tracheo-bronchitis.	*Hæmophilus influenzæ* type B cultured from lung, left ear, trachea and heart blood.	Apparently well previous night, found dead at 6 a.m.
32	M. 3·5 years.	Dead when doctor arrived.	Bilateral hæmorrhagic pleural effusion, hæmorrhagic pericarditis with effusion, blotchy purplish rash on backs of thighs.	Acute tracheo-bronchitis, acute pericarditis, early myocarditis.	Influenza virus type A isolated from lungs and trachea.	Nil.
33	M. 2 years.	Died on arrival at hospital.	Hæmorrhages on surfaces of kidneys, hæmorrhagic suprarenals with disintegration.	Acute tracheo-bronchitis.	Influenza virus type A isolated from lungs and trachea.	Complained of feeling ill eight hours before death. Given "tablets" for inflamed tonsils.
34	F. 2·5 years.	Dead in bed with parents.	Chicken-pox scabs on skin, trachea and bronchi red and injected.	Tracheo-bronchitis.	Not made.	Recovering from chicken-pox, running nose for two days.
35	M. 7 years.	Dead in bed.	Reddened tracheal and bronchial mucosa, gross hæmorrhages in suprarenals.	Tracheo-bronchitis, early meningitis.	Not made.	Examined at 7 p.m. by doctor, child obviously ill, found dead at 11 p.m.
36	M. 6 years.	Died on way to hospital.	Purpuric rash on skin, trachea and bronchi red and congested, extensive suprarenal hæmorrhages.	Tracheo-bronchitis, hæmorrhagic suprarenals.	Smear from skin contained meningococci.	Twenty-four hours before death complained of being ill and was delirious.
37	F. 2 years.	Dead when doctor examined her.	Blotchy rash on skin, hæmorrhagic left suprarenal.	Tracheo-bronchitis, early meningitis.	Staphylococcus coagulase-positive cultured from trachea.	Well till 5 p.m. previous evening, when she vomited; rash appeared next morning.
38	F. 3 years.	Dead in bed.	Spleen a little enlarged and firm.	Acute bronchitis.	*Streptococcus viridans* cultured from heart blood, spleen and brain.	Death preceded by convulsions and vomiting of less than 24 hours' duration. Given 300,000 units of penicillin three hours before death.
39	M. 4·5 years.	Dead in bed.	Reddened, swollen mucosa of larynx and trachea.	Acute laryngo-tracheo-bronchitis.	*Hæmophilus influenzæ* type B obtained in pure culture from heart blood.	For two days slight cold and running nose, six hours acutely ill, vomiting and headache.
40	F. 15 days.	Dead in bed.	Very pale liver.	Acute bronchitis and bronchiolitis.	Not made.	Child had caught chill when coming home from hospital.
41	M. 3 weeks.	Dead on arrival of doctor.	Bilateral internal hydronephrosis, bilateral hydroureter, pyelonephritis.	——	Not made.	On day before death mother was told child was suffering from starvation; whimpering and breathing heavily two hours before death.
42	M. 4 months.	Found dead in cot.	Petechiæ on heart and lungs, typical asphyxial picture.	Acute bronchitis.	Not made.	Apparently well on night before death.
43	M. 7 weeks.	Found dead in cot.	Petechiæ on lungs.	Acute bronchitis.	Not made.	Apparently well.

A specimen of nasal contents was taken by introducing a swab into each nostril alternately. The post-mortem attendant then reflected the skin and muscles over the thorax and abdomen, and removed the sternum by cutting through the costal cartilages on both sides with a non-sterile knife. With sterile instruments the pericardial sac was opened and specimens of pericardial fluid and heart blood were obtained with sterile Pasteur pipettes. The heart blood was obtained by thrusting a fine sterile Pasteur pipette into one of the ventricles, usually about two millilitres of blood being easily obtained. With another set of sterile instruments pieces of liver and spleen were removed. The tongue was then freed and the thoracic viscera were displaced forwards *en bloc*. The thoracic organs were freed

by cutting the diaphragm with sterile scissors. They were then placed on a sheet of sterile grease-proof paper with the untouched posterior surfaces uppermost. To do this only the tongue was handled and used for traction. Pieces of lung, about eight cubic centimetres in size, were cut from near the hilum. Care was taken to avoid contamination of the specimen from the cut end of the œsophagus. The trachea was dissected out from the larynx to the bifurcation and removed aseptically. The cranium was opened in the usual way and the brain shaken backwards to expose the base without touching it. A swab was introduced and material obtained from the base of the brain without touching any other part. The brain was then removed and the middle ears were opened with sterile scissors and a swab was taken from each. A swab was taken from the lumen of the small bowel.

The material was taken to the laboratory with all possible speed and cultures were made. The swabs, blood and pericardial fluid were directly plated on horse blood agar plates and inoculated into cooked meat medium, and these were incubated at 37° C. The trachea was cultured by taking a loopful of scrapings from the respiratory epithelium and inoculating blood agar and cooked meat media. Scrapings from the cut surface of the lung, liver and spleen were similarly cultured.

The blood agar plates were inspected daily for about a week and the various organisms were isolated and identified by their cultural, biochemical and serological reactions. The cooked meat cultures were examined after forty-eight hours and again after one week by the preparation of stained smears and appropriate plating.

The Significance of Bacteria found Post Mortem in Blood and Other Organs.

The bacteriological examination of specimens taken at autopsy is not commonly undertaken. This is probably due to the rather widely held belief that after death there is a fairly rapid invasion of the body by microorganisms from the alimentary canal. However, a search of the literature demonstrated that this view is erroneous. Adamson (1949), in his monograph dealing with bacteriology of lymph nodes, summarized the major studies made on the bacteriology of post-mortem material. Briefly, this review indicated that bacteriological studies of human post-mortem material have been carried out since 1870. Blood cultures made *post mortem* from 4306 cases were found to tally well with cultures made during life, and a critical analysis of 1202 cases showed good agreement between the post-mortem bacteriological findings in the blood and other organs and the infective processes known to have been present during life. Nothing could be found in the literature to suggest that the duration of the agonal period in itself (provided that after death the body was kept at a temperature of about 10° C.) or that the time elapsing between death and autopsy up to a period of ninety-six hours played any real part in the post-mortem bacteriological state of the body.

Burn (1934*a*) systematically examined the question of post-mortem bacteriology. He subjected his findings to statistical analysis, and concluded that bacterial invasion of the body within the first forty-eight hours after death was not a significant factor in explaining the positive cultural results obtained from the various organs. No information pertaining to possible invasion of the blood-stream that may occur immediately prior to or just following death was obtained.

In another paper (Burn, 1934*b*) rabbits and guinea-pigs were inoculated with various pathogenic and non-pathogenic bacteria and then killed. The organs of these animals were examined at various times after death. When the bodies were kept at 10° C. prior to examination no evidence of invasion by the most invasive organisms—namely, *Clostridium welchii*, *Escherichia coli* and staphylococci—could be obtained. At 25° C. and 37° C. invasion by these organisms did occur, but even under these conditions a large group of pathogenic and non-pathogenic bacteria failed to invade other organs when introduced into the right pleural cavity, subcutaneously or into the rectum just before death.

Table II sets out a summary of the bacteriological findings obtained in the present study. The number of cases in which the various organs were examined can be obtained by taking the sum of the positive and negative results in each case.

Cultures of the nasal and tracheal scrapings yielded in some cases intestinal bacteria—namely, *Escherichia coli* and *Streptococcus fæcalis*. This was probably due to the fact that in some children agonal vomiting occurred.

Swabs were taken as a routine measure from the middle ears in 18 of the bodies examined, and cultures were obtained from four; but in one of these (Case 19) the possibility of contamination at autopsy could not be eliminated. In the other three cases pus was found to be present when the ears were opened. In Case 31 *Hæmophilus influenzæ* type B was obtained, in Case 24 a heavy growth of *Staphylococcus pyogenes*, and in Case 13 a pure culture of *Streptococcus pneumoniæ* type IV was obtained. In four other cases—namely, 10, 12, 21, 22—thin mucopus was noted macroscopically at autopsy, but cultural results were negative. In one of these (Case 22) it was subsequently learned that the child had been treated with penicillin and sulphonamide.

Culture of the heart blood gave positive results in six cases. In Case 29 *Staphylococcus pyogenes* was obtained, in Case 15 *Escherichia coli*, in Cases 31 and 39 *Hæmophilus influenzæ* type B, and in Case 13 *Streptococcus pneumoniæ* type IV.

In four of these cases in which a positive result was obtained on heart blood culture, clear evidence of bacterial spread from a defined focus was obtained. We may now consider these cases in detail.

CASE 13.—S.A., a male child, aged four and a half months, had been apparently well and was found dead in his pram with his face downwards in the pillow. Autopsy was undertaken about ten hours after the body was discovered. On macroscopic examination the only abnormality was left *otitis media* and the presence of petechiæ on the heart and lungs. On microscopic examination no definite abnormality was found. The pus from the left middle ear produced a heavy growth of *Streptococcus pneumoniæ* type IV in pure culture. The heart blood also provided a scanty growth of *Streptococcus pneumoniæ* type IV. The remaining cultures were not significant.

The finding of the same serological type of pneumococcus in the middle ear and heart blood strongly suggests that the child suffered an invasion of his blood-stream from the middle ear probably some time before death.

CASE 15.—H.B. was a male child, aged one month. He had been born four weeks prematurely, and his mother had

TABLE II.

Showing the Results Obtained on Culture of the Various Organs.

Nose.		Trachea.		Lungs.		Heart Blood.		Pericardial Fluid.		Liver.		Spleen.		Bowel.		Brain.		Ears.	
Positive.[1]	Negative.[1]	Positive.	Negative.	Positive.	Negative.	Positive.	Negative.	Positive.	Negative.	Positive.	Negative.	Positive.	Negative.	Positive.	Negative.	Positive.	Negative.	Positive.	Negative.
20	1	22	0	18	3	6	16	2	15	1	13	3	19	0	16	3	17	3	14

[1] "Positive", positive cultures obtained of pathogenic or potentially pathogenic organisms; "Negative", no growth obtained.

taken him to a baby health centre because he was vomiting his food. The sister in charge of the health centre advised the mother to take the child to a doctor, as he was suffering from severe thrush infection of the mouth. The mother consulted a doctor, who treated the fungous condition. The child was found dead in his cot the next morning. Autopsy was performed less than ten hours after death. There was increased pericardial fluid, and straw-coloured fluid was present in the abdomen. Advanced thrush infection was found in the mouth and œsophagus. Microscopic examination revealed acute pyelonephritis. Swabs taken from the nose, trachea and lungs yielded a growth of *Escherichia coli* and *Staphylococcus pyogenes*, while the pericardial fluid, heart blood, spleen, liver and brain yielded pure cultures of *Escherichia coli*. Swabs taken from the mouth and œsophagus and sown out on Saboraud's medium provided a growth of *Oidium albicans*.

The bacteriological examination in this case revealed the cause of death as *Escherichia coli* septicæmia. The histological examination disclosed the point of entry of the bacteria causing the septicæmia.

CASE 31.—W.N., a male child, aged six months, was apparently well the night before he was found dead in his perambulator at 6 a.m. Autopsy was carried out about ten hours after he was found dead, and macroscopically the only abnormal findings were a reddened larynx and trachea and left *otitis media*. Microscopic examination revealed acute bronchopneumonia and larygo-tracheo-bronchitis. The cultures from this case yielded *Hæmophilus influenzæ* type B from the trachea, left ear, lung and heart blood. One loopful of the heart blood spread on a blood agar plate produced 30 to 40 colonies of *Hæmophilus influenzæ* after seventy-two hours' incubation at 37° C. The organism was identified by its dependence on the growth factors X and V (Fildes, 1923), and typed by means of the precipitin test with extracted capsular material and specific type sera (Pittman, 1931).

The distribution of the organism in the body suggests that this child died as a result of invasion of his bloodstream with *Hæmophilus influenzæ*, which had been causing his laryngo-tracheo-bronchitis and *otitis media*.

CASE 39.—H.A. was a male child, aged four and a half years. He had a history of having had a "slight cold and running nose for two days". Some six hours before death he was acutely ill with vomiting and severe headache. He was found dead in his bed. Autopsy was performed about twenty-four hours after death, and the only macroscopic finding was reddened, swollen mucosa in the larynx and trachea. Microscopic examination revealed evidence of acute laryngo-tracheo-bronchitis. Swabs taken from the trachea grew *Escherichia coli, Streptococcus viridans, Staphylococcus pyogenes* and *Hæmophilus influenzæ* type B. A similar growth was obtained from the lung. Heart blood plated on blood agar yielded a pure culture of *Hæmophilus influenzæ* type B, and a swab from the base of the brain produced a similar growth. There was no evidence of meningitis, and the growth of *Hæmophilus influenzæ* type B from this situation could be accounted for by the infected blood collected on the brain swab.

Examination for Influenza Virus.

To make the examination for the presence of influenza virus the trachea was split in halves longitudinally and cut into small pieces with sterile instruments. The pieces were then ground with sterile silica in a mortar and about five millilitres of sterile broth were added. The liquid grindings were collected in a tube and allowed to settle under gravity in the refrigerator at 4° C. The lung was similarly but separately treated. Equal parts of the grindings from the trachea and lungs were mixed with penicillin and streptomycin and inoculated intraamniotically into thirteen-day-old chick embryos by the method of Beveridge and Burnet (1946). The embryos were incubated at 35° C. for five days, and then from those remaining alive amniotic fluid was tested for agglutinins with human and fowl red cells. If the result was negative, the chick lungs were ground with sterile sand and the grindings were mixed with amniotic fluid and reinoculated into chick embryos as before.

Failure to detect any abnormality in these embryos or to find any hæmagglutinin in the amniotic fluid or lung grindings was regarded as a negative result. The human lung suspensions were also examined for the presence of complement-fixing antigen by the use of the technique described by French and Donnelley (1951).

In two of the 22 cases examined (32, 33) a type A influenza virus was isolated.

FIGURE I.

CASE 32.—The subject was a male child, aged three and a half years. He had had his tonsils removed one month previously. There was no history of illness prior to his being found dead. The autopsy was performed seventeen hours after the child was found dead. Macroscopic examination revealed acute hæmorrhagic pericarditis and a hæmorrhagic pleural effusion on both sides. A blotchy purplish rash was present on the back and over both thighs. On microscopic examination acute tracheo-bronchitis, acute pericarditis and myocarditis were found.

Cultures yielded no significant findings despite a careful attempt to cultivate the meningococcus. A strain of influenza virus type A was isolated in chick embros, and an emulsion of the child's lungs proved to be anticomplementary (French and Donnelley, 1951).

CASE 33.—A male child, aged two years, had complained of feeling ill for eight hours before death. He was examined by a doctor and given "tablets", presumably of a sulphonamide. His condition became rapidly worse and he was taken to hospital but was found to be dead on arrival there. At autopsy, which was performed nine and a half hours after death, the significant macroscopic finding was intense hæmorrhagic disintegration of the suprarenals of the type associated with the Waterhouse-Friedrichsen syndrome. Hæmorrhages were also seen on the surface of both kidneys. Other organs were apparently normal. Microscopic examination revealed acute tracheo-bronchitis. No significant bacteria were obtained in culture despite careful attempts to cultivate the meningococcus. From the trachea and lungs an influenza virus type A was isolated, and the lungs were found to contain a high titre of complement-fixing antigen of type A influenza virus. This result indicated that influenza virus had been growing in the lung for at least two days before death (Donnelley, 1950; French and Donnelley, 1951).

EPIDEMIOLOGICAL FINDINGS.

The observation that these cases of unexpected death in young children tend to be more frequent at certain times of the year, especially the winter months, is supported by an

TABLE III.

Group I. "Adequate" Cause for Death Established.		Group II. Cases with Doubtful Pathogenesis.	
Cause of Death Established by Pathological or Bacteriological Methods.	Viral-bacterial Syndrome.	Respiratory Tract Infections.	Non-respiratory Infections.
Cases 1, 4, 13, 15, 24, 29, 31, 39, 41.	Cases 7, 8, 10, 16, 32, 33, 35, 36, 37.	Cases 2, 3, 6, 9, 11, 12, 14, 17, 18, 20, 21, 22, 27, 28, 30, 34, 38, 40, 42, 43.	Cases 5, 19, 23, 25, 26.

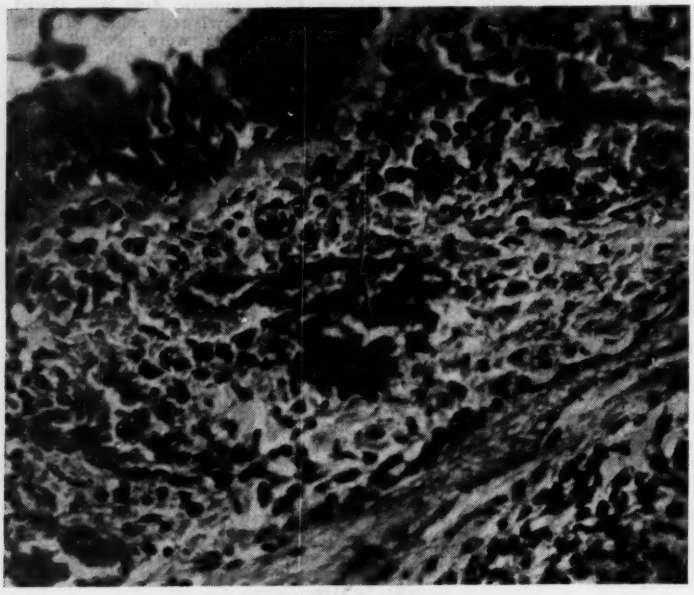

FIGURE II.

Photomicrograph. Section of the trachea in Case 36 showing acute tracheitis. The infiltrating cells are predominantly mononuclear, most of them being plasma cells. Death was due to meningococcal septicæmia. (Hæmatoxylin and eosin stain.)

examination of the figures over the past two years. Figure I shows the monthly incidence of unexplained "sudden death" of babies, aged under eighteen months, brought to the morgue over a period of two years (1948 to 1950).

It is evident that there is a significant increase in the number of these cases in the winter months of May, June and July. This is what would be expected if respiratory infections played a major part in causing these deaths. On the other hand, it is hard to see why there should be any seasonal variation in the number of deaths if mechanical suffocation was a cause. Werne and Garrow (1947) and Rabson (1949), working in the northern hemisphere, also noted a peak in the incidence of unexpected deaths in infants coinciding with the winter months.

DISCUSSION.

The present investigation was undertaken with two objects in view. It was hoped to obtain further evidence for the previously stated thesis that normal healthy children do not die by accidental mechanical suffocation by bed-clothes, and by means of bacteriological and virological studies it was hoped to throw some light on the mechanism of the cause of death.

The 43 cases studied during the year 1950 may be divided into two main groups, each with a subgroup. In the first group are those cases in which investigation established what could be reasonably regarded as an adequate cause of death. In the second group are those cases of particular interest in which the histological findings would be regarded by most pathologists as insufficient in themselves to establish the cause of death. These are further divided into those in which evidence of respiratory infection was found, and a small rather heterogeneous group without such evidence.

Table III sets out the grouping of the cases on this basis.

The inclusion of the five cases of septicæmia (13, 15, 29, 31 and 39) in the first group is based upon our belief in the accuracy of post-mortem bacteriological studies. All the bacteriological evidence obtained in the present study is consistent with the findings of other investigators who have made post-mortem bacteriological examinations. Of the 22 cases in which culture of the heart blood was undertaken, 16 gave negative results, which in itself is a reasonable control on the series. It may be objected that our positive findings represent agonal invasion of the blood-stream. Evidence against this view is provided by Case 24. This child died in the country and autopsy was performed approximately sixty hours after death. In spite of the presence of extensive staphylococcal bronchopneumonia, bronchiectasis and bilateral *otitis media*, culture of the blood gave negative results. The child had received no antibiotic drug or any other treatment prior to death. The two cases (31, 39) of *Hæmophilus influenzæ* type B septicæmia are similar to cases described by Sinclair (1941) in America and Navasquez (1942) in England. These workers both described *Hæmophilus influenzæ* type B septicæmia as a complication of acute laryngo-tracheo-bronchitis. Navasquez also obtained a positive result on blood culture *post mortem* in his case.

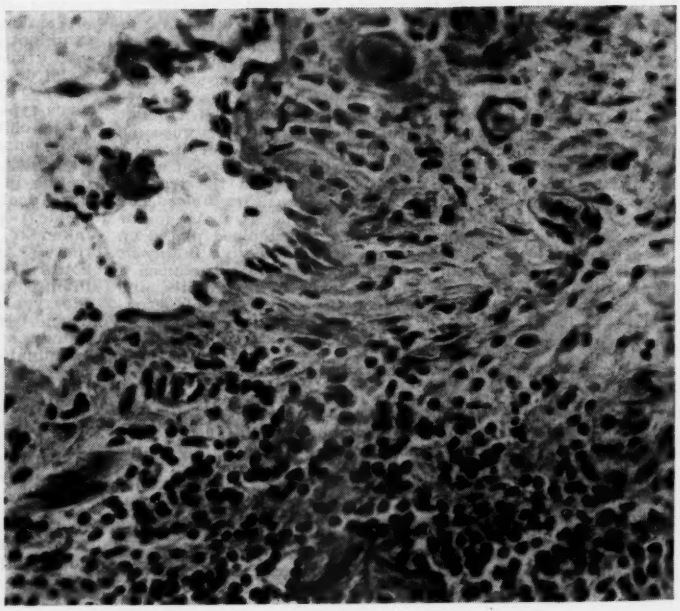

FIGURE III.

Photomicrograph. Section of a large bronchus from Case 33. Note destruction of the bronchial epithelium and mononuclear infiltration of the bronchial mucosa. There were numerous plasma cells and a few eosinophile cells. Influenza virus was isolated in this case. (Hæmatoxylin and eosin stain.)

The second subgroup of the first group, comprising nine cases (7, 8, 10, 16, 32, 33, 35, 36, 37), make what we have called the viral-bacterial syndrome. In all these cases a blotchy macular rash was present on the body *post mortem*, and in five of them (7, 33, 35, 36, 37) the adrenals were hæmorrhagic, while evidence of meningitis

was found on microscopic examination in three cases (10, 35, 37).

In Case 8 thin, purulent pericarditis was present (see Figure VI). Meningococci were demonstrated by Gram's stain, and a growth of *Neisseria meningitidis* type I was obtained by cultivation of the pericardial pus on blood agar under increased carbon dioxide tension. Examination of a smear of the skin rash in Case 36 revealed numerous intracellular meningococci, but in this case no other bacteriological examination was carried out, cultures being attempted only in six (8, 10, 16, 32, 33, 37) of the nine cases.

The failure to demonstrate the meningococcus in all these cases may be due to two reasons. The bodies of these children were all examined as soon as possible after their arrival in the morgue, but nevertheless it was usually about twelve hours or more after death that cultures were made. It is well known that meningococci die out rapidly at temperatures below 37° C. (Topley and Wilson, 1946). Then again it is perhaps unfortunate that penicillinase and para-aminobenzoic acid were not as a routine measure included in the media used for the attempted cultivation. In Case 33 sulphonamide tablets had been given by a doctor a few hours before the patient's death.

Histologically the upper part of the bronchial tree in all these nine cases presented a similar picture. Figures II, III and IV were prepared from three of these cases, and in all a mononuclear type of infiltration was present, perhaps more suggestive of virus than of bacterial infection.

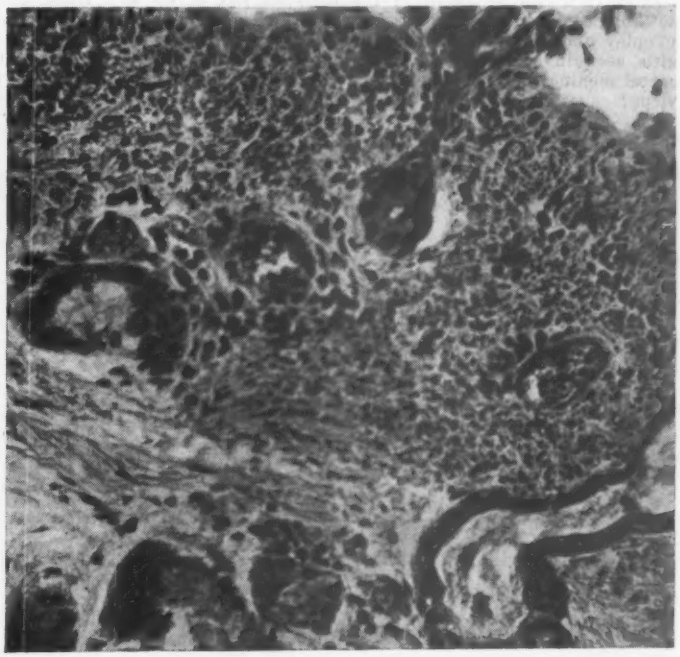

FIGURE IV.

Photomicrograph. Section showing acute tracheitis in Case 8. The epithelium is largely destroyed. The infiltration is predominantly mononuclear; the plasma cell prevailed. (Hæmatoxylin and eosin stain.)

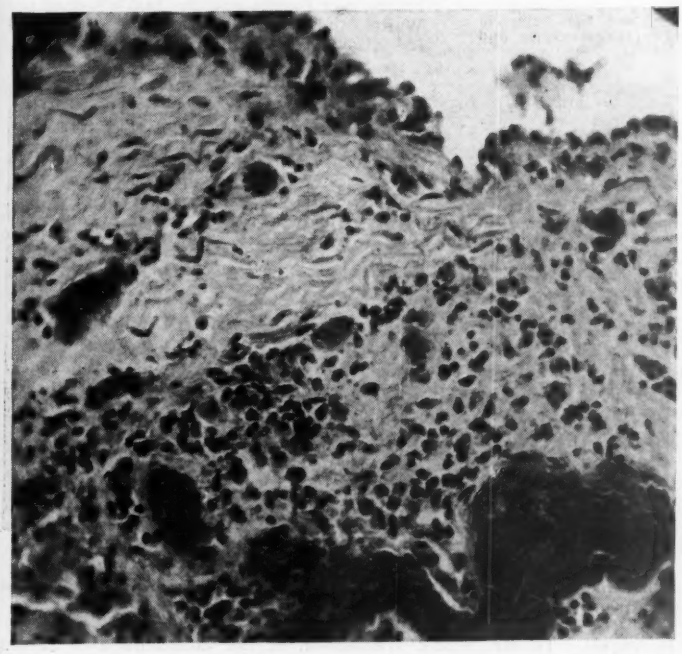

FIGURE V.

Photomicrograph. Wall of a large bronchus from Case 21, showing some denudation of respiratory epithelium, engorged blood vessels and infiltration of the bronchial mucosa by mononuclear cells. (Hæmatoxylin and eosin stain.)

The plasma cell predominated. It may be remarked here that in all these cases in which the macroscopic appearances suggested meningococcosis, no meningococci were demonstrable in sections of the trachea and bronchi appropriately stained. On macroscopic examination Case 33 appeared to be one of meningococcosis, but Figure III shows histological appearances in the bronchial tree of this child more suggestive of a virus infection than of infection by the meningococcus. In addition the lungs were found to contain a high titre of complement-fixing antigen of the type A influenza virus. Furthermore, a strain of influenza virus type A was isolated from the trachea of this subject in eggs. Whatever interpretation is placed upon the macroscopic findings, there can be no doubt that influenza virus had been multiplying in the lungs of this child for some time before his death (French and Donnelley, 1951). The same remarks are applicable to Case 32.

In view of the similarity of the microscopic findings in the trachea and bronchi in these children, it would seem not unlikely that two infectious processes were at work, although in no instance were we able to isolate influenza virus and the meningococcus from the same subject. Virus infection of the respiratory tract may be the means of opening the way for fatal meningococcal septicæmia in those children carrying this organism in the naso-pharynx or becoming infected during or after their virus infection. Such a state of affairs is consistent with the known natural history of meningococcal infections. During epidemics of meningococcal infection *Neisseria*

meningitidis can be found in the naso-pharynx of up to 80% of people, some of whom show overt naso-pharyngitis (Topley and Wilson, 1946). Could not the rhinopharyngitis seen in some people during epidemics of meningococcal meningitis be caused by infection with a respiratory virus?

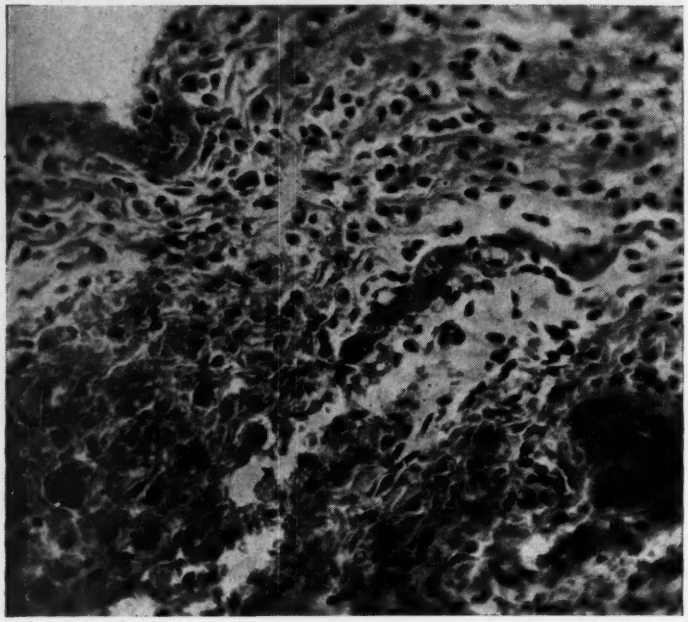

FIGURE VI.

Photomicrograph. Acute meningococcal pericarditis in Case 8. *Neisseria meningitidis* type I was cultivated from this exudate. (Hæmatoxylin and eosin stain.)

The 20 cases in the second group listed under "respiratory tract infections" in Table III are of particular interest. Bacteriological studies were made in only nine of these cases and no significant organism was cultivated. The histological examination in all of them revealed changes similar to those illustrated in Figure V. Case 21 was typical of this group.

This child, aged ten months, the son of a doctor, was examined by a pædiatrician at 4 p.m. one afternoon for a routine "check-up" of his feeding. No serious abnormality was noted about him at the time. At 7 a.m. on the following morning his mother found him lying face downwards, dead, in his cot. Examination of sections of a large bronchus (Figure V) revealed some denudation of the respiratory epithelium, engorgement of the blood vessels, and œdema and infiltration of the bronchial mucosa by mononuclear cells. Subsequent inquiry revealed that two older children in the house were recovering from respiratory tract infections at the time of their brother's death.

The majority of cases in this investigation showed evidence of respiratory tract infection, and this can be regarded as a reflection of the prevailing infections in the community during 1950. During the months of May to August influenza, due to influenza virus type A, was epidemic in the community (Anderson, French and Kalra, 1951).

Attempts to isolate influenza virus were made in the nine cases (9, 11, 12, 17, 18, 20, 21, 22, 38) subjected to bacteriological study. In none was this virus isolated. When the epidemiological conditions are favourable for the spread of influenza virus it is highly likely that they are also favourable for the spread of other respiratory viruses that cannot be detected by laboratory means. Dingle (1948) has described a series of human pathogenic viruses which can be demonstrated only by use of human volunteers and which produce pathological changes that are no more extensive than those illustrated in Figure V. In this group definite histopathological changes were demonstrated in the respiratory tract, but the bacterial or viral ætiological agent was not isolated. Although these changes may be regarded by many pathologists as inadequate demonstration of the cause of death, they do indicate that the respective children were suffering from a disease (and that they did not mechanically suffocate). It may be that more refined techniques will in future allow the isolation of the micro-organisms responsible for cases similar to those belonging to this group.

A small group of cases in this particular series were non-respiratory (5, 19, 23, 25, 36). Here again it is evident that we are dealing with infections, but the techniques used were inadequate to allow the identification of the infecting organism.

CONCLUSION.

In our opinion the explanation of these sudden deaths is not to be found in mechanical factors, but in disease processes which are frequently discoverable only by careful investigation. It will be found that these sudden deaths in infancy are largely a reflection of the prevailing diseases in the community at the particular time.

ACKNOWLEDGEMENTS.

We wish to express our thanks to Sir Macfarlane Burnet and Dr. Ian Wood, of the Walter and Eliza Hall Institute of Medical Research, for their interest and suggestions.

To Mr. Frank Warburton, of the Commonwealth Serum Laboratories, Melbourne, we are grateful for a gift of sera used in the typing of the *Hæmophilus* strains. Mrs. Margaret Donnelley, of the Walter and Eliza Hall Institute, carried out the complement fixation tests for influenza. Thanks are also due to Mr. H. Quigley, technician at the

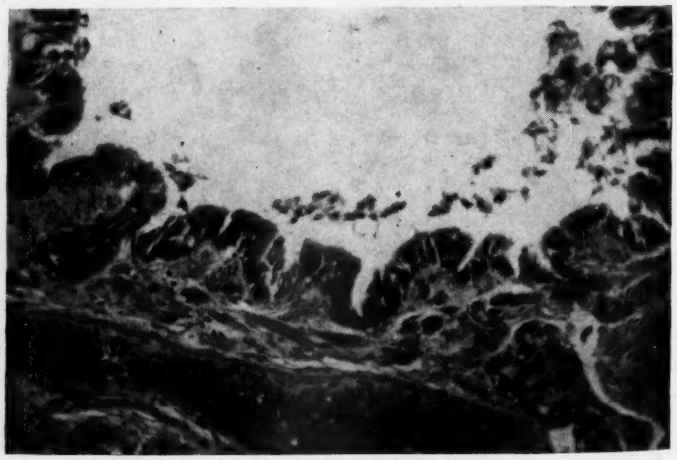

FIGURE VII.

Photomicrograph. Normal trachea of a child for comparison with Figures II, III, IV and V. (Hæmatoxylin and eosin stain.)

City Morgue, and to Mr. J. Guthrie, of the pathology department, University of Melbourne.

SUMMARY.

1. A further series of 43 cases of unexpected death among infants and young children is reported; this includes a large proportion in which death by suffocation in bed was suspected.

2. In addition to macroscopic and microscopic examination, systematic cultural studies were made in twenty-two of the cases. These included attempts to isolate influenza virus from respiratory tissues.

3. A combination of methods established an "adequate" cause for death of infective nature in 14. In these there could be no question of "accidental death from suffocation".

4. There is a large group (20 cases) in which histological evidence of respiratory tract infection can be found, but in which the ætiological agent was not isolated.

5. Only two cases of proven meningococcal infection were discovered, but a number of others (seven) showed features strongly suggestive of acute meningococcal infection, but with negative cultures. It is of interest that from two of these influenza virus was isolated.

6. The seasonal incidence of these unexpected deaths suggests that respiratory infection (or some factor correlated with the incidence of respiratory infection) is an important causative agent. This fact is borne out by the following: (*a*) There is a well-marked peak of these deaths in the winter months April to July. (*b*) In many of the cases careful inquiry revealed histories of mild respiratory infections for a few days previously, or associated infections in the family. (*c*) Histological evidence of tracheobronchitis and acute bronchitis is extremely common (29 cases). (*d*) *Otitis media* was found in seven cases.

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THE RARE A_3 AGGLUTINOGEN.

By R. J. WALSH and the late RUTH HERZGER.[1]

From the New South Wales Red Cross Blood Transfusion Service, Sydney.

FISCHER AND HAHN (1935) reported the finding of a patient of blood group A whose red cells were very weakly agglutinated by strong anti-A grouping serum. In the following year Friedenreich (1936) observed the same phenomenon in six out of a series of 4000 patients investigated. Family studies of 260 relatives of these six subjects disclosed a further 46 examples. To explain his findings Friedenreich postulated a further allelomorph of the principal blood groups and termed this A_3. His family studies demonstrated the inherited character of the A_3 allelomorph, and showed that both A_1 and A_2 mask the presence of A_3 in the same manner as A_1 masks the presence of A_2.

Recently Moullec and Diacono (1950) reported a further instance which came to their notice and studied 41 members of the family. The A_3 agglutinogen was detected in 10 members. These authors quote nine other published examples, but the frequency of A_3 is very low. A further family was recently investigated in Australia.

Investigation.

The blood groups of the patient and of the members of her family, who are of British descent, are shown in Figure I.

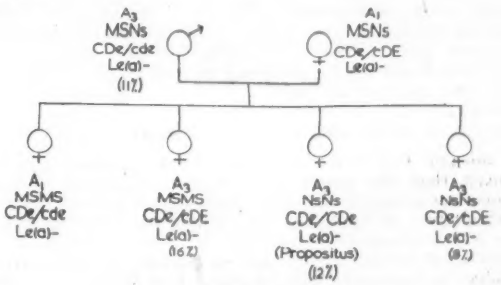

FIGURE I.

When strong anti-A serum was mixed with red cells of the group A_3 members, only a proportion of the cells were agglutinated. Microscopically the appearance was similar to that seen when a mixture of group O and group A cells is treated in the same manner. Both the propositus and the next sibling were secretors of group A substance, their saliva inhibiting the action of group B serum against A_1 and A_2 cells. The sera of all four group A_3 subjects contained β agglutinins of average titre, but no α or α_1 agglutinins, and in no instances were the cells agglutinated by anti-A_1 agglutinins.

In all four group A_3 subjects the percentage of red cells agglutinated by anti-A serum is shown in parentheses in the figure. This was determined by performing a red cell count in the usual manner on a suspension of cells from the subject. A second red cell count was performed on the same suspension, but strong anti-A serum was used instead of red-cell diluting fluid, and only the unagglutinated cells were counted. The difference between the two counts represented the agglutinated cells and was expressed as a percentage of the total. The results on all four subjects may be considered identical within the limits of the experimental error. Similar counts by the use of the same anti-A serum on cells from an A_1 subject and from an A_2 subject gave figures of 96% and 88% respectively.

The question arose as to whether the unagglutinated cells had absorbed anti-A agglutinins. The addition of anti-human globulin serum (Coombs serum) to washed group A_3 cells, which had previously been mixed with

[1] Died June 12, 1950.

anti-A serum, did not increase the number agglutinated. Furthermore, suspensions of cells in serum instead of in saline prior to mixing with anti-A serum did not increase the agglutination. Serum of group O subjects was not more effective in this regard than was serum from group B subjects.

The cells of one group A_3 subject gave much stronger reactions with two anti-H sera than did the cells of two group A_1 subjects and of one group A_2 subject. The scoring method used by Race and Callender (1946) gave the results shown in Table I.

Discussion.

The practical importance of the A_3 allelomorph is that its presence may be overlooked and the patient's blood incorrectly grouped. This is especially likely to occur if high-titre and anti-A serum is not used.

The characteristic feature is the selective agglutination of a minority of the red cells. The high-titre grouping serum used in this investigation was prepared by injecting blood-group polysaccharides A and B into volunteers, and was shown to contain both complete and incomplete anti-A agglutinins reacting against both A_1 and A_2 cells. No evidence could be obtained that the incomplete form of agglutinin was attached to the unagglutinated cells. The cells therefore appear to react as group O cells, but there is no direct evidence that they do in fact contain a double dose of the O antigen and that the phenotype is OO.

TABLE I.

Titration Scores of Anti-H Serum.

Cells.	Anti-H Serum I.	Anti-H Serum II.
A_1	15	5
A_1	28	7
A_2	43	25
A_3	53	35

Morgan and Watkins (1948) have advanced the hypothesis that the genes A, B and O represent mutations from the primary or basic blood group gene H, and that the degree of mutation determines the relative amounts of A and H substances present in group A red cells. The finding of a high titre of anti-H against the group A_3 cells tested is consistent with the view that the A_3 gene characteristics result from a minor degree of mutation, the cells containing a relatively small amount of A substance and a large amount of H substance. However, this suggestion does not explain the inagglutinability of the majority of the cells with anti-A serum, because even if the postulated mutation is only partial, it may be expected to affect all the red cells. It should be mentioned that selective agglutination was not observed with anti-H or any other testing serum.

Summary.

The rare blood group A_3 was investigated in four members of a family. Only a minority of the red cells of these subjects were agglutinated by powerful anti-A serum, and the subjects may be incorrectly blood grouped. The cells were not agglutinated by a_1 (anti-A_1) agglutinins, but reacted strongly with anti-H serum. The relationship of the A_3 gene to the basic blood group gene H is discussed.

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A SURVEY OF AUSTRALIAN ABORIGINES FOR PULMONARY TUBERCULOSIS.

By ALAN KING, GREY EDWARDS AND PETER GIBSON,

Perth.

IN the months August to November, 1950, a survey was carried out on some 3200 natives of the Kimberley and Port Hedland districts of Western Australia by staff from the Tuberculosis Control Branch of the Department of Public Health.

Owing to the nature of the country and isolation of many of the missions and stations, aerial transport was used for the greater part of the survey. In the Broome area the survey was made by road.

For the most part the survey team consisted of one medical officer and one X-ray technician (increased at the beginning of the survey and later for a short overlap period during changeover of personnel).

A standard 85/30 portable X-ray unit was employed taking 17-inch by 14-inch films, together with a portable generator, cooling unit and dark room. The total weight of equipment was less than 1400 pounds.

Altogether, 26 centres were visited, covering seven missions, 46 sheep and cattle stations and five towns—Wyndham, Derby, Broome, Fitzroy Crossing and Marble Bar. At Wyndham, Derby and Broome the X-ray unit of the local district hospital was used.

An approximate area of 200,000 square miles was covered and the extent of this is roughly outlined in the following map (Figure I).

Numbers Examined.

A total of 3209 natives was examined.

Mantoux tests were carried out on 2657.

B.C.G. vaccine was given inadvertently to 1087 non-reactors under the age of forty-five years.

Radiological examination of the chest was carried out on 1191 positive reactors.

X-ray examination without preliminary Mantoux testing was carried out on 555 (this included 270 at the Derby leprosarium).

Incidence of Pulmonary Tuberculosis.

Significant radiological evidence of pulmonary tuberculosis was discovered in 15 cases.

Of these, two were of active infections (including one case of miliary tuberculosis), one was of a mixed type of lesion and 12 were of predominantly fibrotic type.

Minor radiological abnormalities were noted in 21 other cases; some of these are considered suspects requiring further observation.

The over-all incidence of pulmonary tuberculosis of less than five per thousand, especially in view of the type of lesion found, does not appear to be an unduly significant finding, and represents a lower incidence of the disease than in the white population.

In one particular area four proven positive fatal cases had been reported previously in 1948-1949, and it was here that the survey team found a relatively high percentage of cases with significant radiological evidence of disease. In two of these cases designated as tuberculous the patient died one week after the team left the centre, before admission to a native hospital could be arranged. Death was presumably due to pulmonary tuberculosis. The Mantoux conversion rate in this particular area, however, did not show any significant variation from the over-all rate.

Mantoux Conversion Rate.

The standard Mantoux test was employed, 0·1 millilitre of 1:1000 dilution of old tuberculin being injected intradermally. The results did not show any striking dissimilarity from those of the white population.

The following is a comparison made with a survey of the Perth metropolitan area in 1949 (Table I).

The lesser percentages of positive reactors amongst aborigines (with the exception of the nought to five years age group) is as would be expected in a white rural community.

The rate in the aboriginal nought to five years age group is, of course, high, but was due to a preponderance of positive reactors at one Native Affairs Department station (Moola Bulla). No active cases of pulmonary tuberculosis were found here, and there are no milch cows on the station, so there was no apparent cause for this rate.

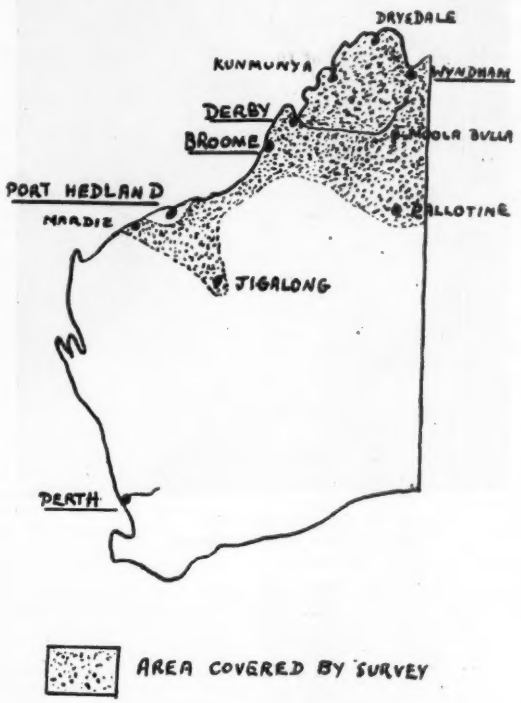

FIGURE I.

Map of Western Australia showing the area covered by the survey.

Effect of White Contact.

Owing to the widely scattered location of groups tested and sparseness of the white and native populations, it is not possible to make more than a few generalizations on the effect of contact of natives with whites. As expected, desert-type natives had a very low conversion rate in contrast to town natives or those who had otherwise had frequent opportunity for white contact. An example is shown in Table II.

Jigalong is a mission situated on the edge of the desert 252 miles south-east of Port Hedland. The only contact with Europeans is the small mission staff.

Pallotine is similarly isolated 134 miles south of Hall's Creek and 326 miles south of Wyndham, where contact with whites is even less. Group A consists of original desert natives at this mission. Group B consists of natives recently transferred from Beagle Bay, a coastal mission north of Broome.

TABLE II.

Location.	Number Tested.	Percentage of Reactors.
Group 1:		
Jigalong	128	22
Pallotine (Group A)	70	21
Group 2:		
Derby area	174	51
Broome town	110	40
Pallotine (Group B)	13	70

B.C.G.

The delivery of B.C.G. vaccine used during the survey is an interesting aspect of modern preventive medicine.

This vaccine has a limited viability, but flown from Melbourne to Perth in the daytime it continued on its way the same night, arriving in the far north of Western Australia within twenty-four hours after leaving Melbourne. The forwarding of vaccine was timed to coincide with the aerial "station run" and on some occasions special feeder and refuelling trips. Pre-cooled vacuum flasks were used from Perth onwards, and refrigeration was available on arrival at the destination.

Follow-up Mantoux testing was not carried out during the survey, owing to the necessity of moving on to other centres, but it is expected that this will be done.

Acknowledgements.

Our thanks are due to the Commissioner of Public Health, Dr. Linley Henzell, for permission to publish this article; to the Commissioner of Native Affairs, Mr. R. G. Middleton, for the cooperation extended by his department; to the operations manager and pilots of the MacRobertson-Miller Aviation Company for their outstanding help in a difficult itinerary; to the various superintendents of the missions; to station owners and managers for their helpful cooperation; and, last but not least, to the technicians of the Department of Public Health who assisted the medical officers under often very trying conditions.

TABLE I.

Comparison of Results of Mantoux Testing of Natives in North-West Survey, 1950, and of Whites in Perth Metropolitan Area Survey, 1949.

Age Group. (Years.)	Results of Mantoux Test.							
	North-West Survey of Natives, 1950.				Perth Metropolitan Area Survey, 1949.			
	Positive.	Negative.	Total.	Percentage Positive.	Positive.	Negative.	Total.	Percentage Positive.
0 to 5	34	256	290	11	—	—	—	—
6 to 10	66	242	308	21	222	548	770	29
11 to 15	101	144	245	41	1216	1084	2300	53
16 to 20	134	100	234	57	268	146	414	64
21 to 25	96	106	202	47	188	71	259	73
26 to 30	152	94	246	61	209	53	262	80
31 to 35	79	56	135	58	174	45	219	79
36 to 40	74	64	138	53	154	45	199	77
41 and over	455	404	859	53	—	—	—	—

MAFUCCI'S SYNDROME: WITH A REPORT OF A CASE.

By HOWARD HALPER, D.M.R.E. (Cantab.), and
LEIGH WEDLICK, M.R.C.P. (London),
The Department of Physical Therapy, Royal Melbourne Hospital, Melbourne.

IN this modern age, collector's pieces in medicine as in art are perhaps more interesting than utilitarian. Although it is probably only of academic value, we are describing what appears to be the first case reported in Australia of Mafucci's syndrome.

Description of Syndrome.

Mafucci's syndrome is an extremely rare condition, and was first described by Mafucci in 1881. In 1942 Carleton *et alii* reviewed the 18 cases which had been reported up to that time, and described two more cases. Since then

FIGURE I.
Photograph of patient, front view.

FIGURE II.
Photograph of patient, back view.

(as far as can be ascertained) a further three cases have been recorded. Krause reported the first American case in 1944, and other cases were reported by King and Kuzma in 1948 (United States of America), and by Nardell in 1950 (England).

Mafucci's syndrome is a non-hereditary mesodermal dysplasia probably arising at an early stage in fœtal life, in which numerous defects in cartilage-bone formation (dyschondroplasia or Ollier's disease) are found in association with multiple hæmangiomata.

The age of the patients at the date when the cases were recorded varied from eight to fifty-eight years; 16 were male and seven female. The patients are of small stature, but of normal intelligence. The bones most frequently involved are the long bones of the arms and legs. Multiple enchondromata are common in the phalanges.

The typical history (adapted from Carleton *et alii*, 1942) is as follows. The patient is usually normal at birth. During the years before puberty small hard nodules begin to appear, usually on one of the fingers or toes. This process is followed by the appearance of dilated veins and bluish tumours, or of soft tumours which show

FIGURE III.
Photograph of hands.

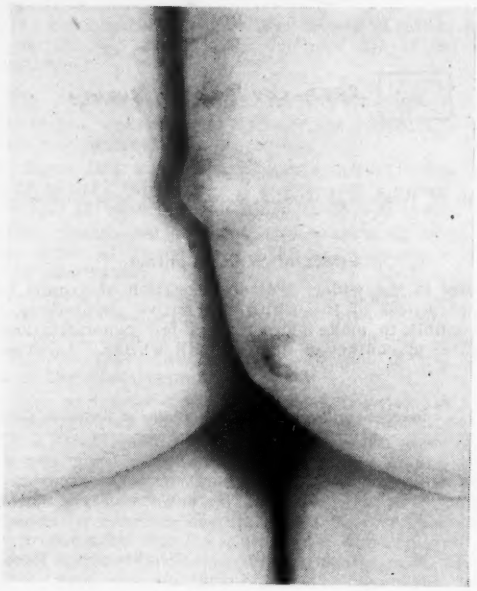

FIGURE IV.
Photograph of buttocks, showing two hæmangiomata.

no skin coloration, but which are also of vascular nature. Their distribution is usually extremely asymmetrical. Fractures may occur after trivial injuries, and union is slow. As growth proceeds the tumours increase in size,

and others appear. The enchondromata of the phalanges become much more pronounced, and may cause hideous deformities. Some of the long bones develop unequally, causing further deformity, and asymmetry becomes more apparent.

When growth ceases the lesions tend to become much less active; but injury may cause exacerbation of cartilage growth or the appearance of new tumours. Malignant changes are not uncommon in the later stages.

Radiological Findings.

Radiological findings may be divided into (*a*) bony changes (primary and secondary) and (*b*) soft tissue changes.

The bony changes are those of dyschondroplasia (Ollier's disease) and may be summarized as follows.

There are numerous irregularly spaced cyst-like areas in the diaphysis associated with cortical expansion. At the end of the involved long bones there are longitudinal strands of unaffected bone about a quarter of an inch in width, and between these are translucent areas of cartilage. These translucent areas may contain small, heavily calcified opaque areas. In the phalanges of the hand multiple enchondromata and ecchondromata are present, more pronounced on one side. The phalanges of the feet are only slightly affected, if at all. As the bones grow, the inhibition of growth in the involved portions of the long bones, and the normal development of the rest of the bone, result in severe deformity. Further postural deformities may then occur, such as *genu valgum, pes planus et cetera.*

FIGURE V.

X-ray picture of chest. Heavily calcified bodies are seen, particularly in the anterior part of the fourth and fifth left ribs.

Distinct from the soft-tissue changes due to cortical expansion from the chondromata, there are numerous soft - tissue swellings due to the hæmangiomata. Typically these consist of rounded areas of increased density in the soft tissue containing calcified phleboliths. Not all the hæmangiomata contain calcified phleboliths; their presence depends upon the age of the lesion. In the foot they are nearly always present, since foot tumours are usually the oldest.

Report of a Case.

J.S., a female patient, aged twenty-four years, is a telephonist. Her mother died of meningitis at the age of twenty-two years; her father is alive and well; one sister, aged twenty-two years, is alive and well; the maternal grandmother had an angioma on the right side.

The patient was a normal baby at birth and was delivered normally. She suffered from measles and from scarlet fever at the age of two years. The menarche occurred at the age of fourteen years. As a child she grew normally until the age of three years, when it was noticed that her nose bled frequently, and that her hands were slightly deformed. At the age of five years the first tumour appeared —a red lump one inch in diameter in the right axilla. This bled frequently, and was excised. A small similar nodule appeared under the left breast, and then small lumps began to appear on the feet; some of these were red, and others were not coloured. At the age of seven years, in a slight fall she fractured the middle of her left femur, and was in hospital for three months. Meanwhile the tumour under her left breast was steadily increasing in size; it was excised at the age of ten years, when it had reached the size of a cricket ball.

Other lumps continued to appear, some of them with normal skin, and others with a bluish-red colour.

At the age of fourteen years, after a minor injury, she refractured her left femur, which on this occasion took six months to heal.

On January 24, 1946, she presented at the out-patient department. Numerous vascular lumps were present, some of them painful, located mainly over the feet, the left breast, the neck, the right side of the palate and the right thigh. Bilateral *genu recurvatum* was present, with pronounced grating in the left knee. Shortening was present in both humeri, with gross deformities and shortening of both forearms and of the phalanges of both hands. The radiological report was as follows:

> Widespread abnormalities in development of bones of a dyschondroplasia type. The hands show gross changes with much deformity of metacarpals and phalanges by enchondromata and ecchondromata. The forearms also are markedly abnormal; they are extremely short with medial and posterior curvature of the left ulna which contains some small chondromata. The radius is even shorter, with poor development of its upper end which is situated some distance from the humerus. The lower end of the radius is large and deformed, and shows chondromatous changes. The bones of the right forearm are deformed and curved, and the ulna is very short, the lower end being well above the wrist joint. The poorly formed head of the radius is dislocated laterally and posteriorly. The *sella turcica* is small, and the clinoids and *dorsum sellæ* have a roughened outline, and are of abnormal bone structure. The rest of the skull is not obviously abnormal. The bones in the region of the knees show some deformity and multiple superchondromata.

The patient was admitted to hospital on February 25, 1946, for excision of hæmangiomata of the feet.

On September 18, 1947, she reported with irregular growth of the right thumb nail, due to a small tumour causing irregular growth at the base. The nail was sharply ridged and partly bifid. One cartilaginous tumour of the left wrist was becoming larger, and a disability.

On May 10, 1948, she complained of aching feet. The pain was diffuse, with no localizing signs. Further X-ray examination of the feet and legs revealed no change from the previous findings on January 24, 1946. She was referred for physical therapy, but obtained no relief.

On May 26, 1950, an enlarging tumour was present at the upper end of an operation scar between the breasts. This tumour was excised, and the pathological report was as follows: "Very vascular nodule. Fibrous tissue only between the blood vessels."

The patient's condition is now (December, 1950) as follows. She is a small, attractive, intelligent girl of twenty-four years, who carries out her duties as a telephonist without difficulty. She is five feet high, and states that she bruises

easily. As is shown in the photographs, considerable asymmetrical shortening and deformity are present in both arms. Pronounced *genu valgum* is present in the left knee, with shortening of the left leg. The measurements are as follows:

	Right.	Left.
Acromion to lateral condyle of humerus	11 inches	7 inches
Lateral condyle of humerus to radial styloid	6¾ inches	8 inches
Anterior superior iliac spine to lateral condyle of femur	18 inches	18 inches
Lateral condyle of femur to lateral malleolus	14 inches	13 inches

FIGURE VI.

Skiagram of forearm and hand. Deformities of the radius and ulna are shown, with enchondromata and ecchondromata.

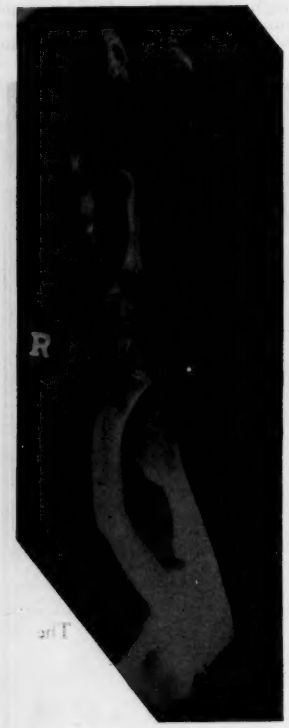

FIGURE VII.

Skiagram of forearm and hand. Deformities of the radius and ulna are shown, with enchondromata and ecchondromata.

Two types of tumours are present. The first has a bluish-red colour, and examples are found as follows: (i) a small angioma, measuring three-eighths of an inch by one-quarter of an inch in the throat, half an inch above the right tonsil; (ii) a tumour half an inch in diameter above the right sterno-clavicular junction; (iii) a tumour one inch in diameter below the acromio-clavicular joint; (iv) a tumour a quarter of an inch in diameter above the lower end of the left humerus; (v) a tumour two inches in diameter below the left knee joint; (vi) three tumours on the left buttock; (vii) two tumours on the right buttock, half an inch in diameter; (viii) a tumour on the plantar aspect of the foot. The second type of tumour without skin discoloration is found on both hands, more on the left than on the right, and on both feet.

Scars are present where tumours have been excised from the following sites: the base of the tongue, the back of the neck, the left hand, both feet, beneath the left breast (a small keloid in the scar), in the right axilla and between the breasts.

Radiological Findings.

On November 28, 1950, a radiological examination revealed the following bone changes. In the ribs, expansion of the anterior parts of the first, second, fourth and fifth right ribs was noted near the costo-chondral junction, and also of the second, fourth and fifth left ribs (particularly the fifth) in the same region. These expanded areas contained heavily calcified bodies. In addition numerous small radiolucent areas were seen in the lower ribs on both sides. The clavicles appeared normal. The scapulæ were deformed, and in them numerous radiolucent areas containing calcified bodies were seen. The right humerus was somewhat abnormal in shape, but not grossly so, and contained a few small radiolucent areas. At the lower third it became narrow. It was of normal length for the size of the patient. The left humerus was very small and of abnormal shape. The head and upper third were expanded and contained radiolucent areas and calcified bodies, and there was linear striation of normal bone between these areas. The right radius and ulna were both short and abnormal in shape and contained radiolucent areas, mainly confined to the distal ends. The radius was longer than the ulna, and the head of the radius did not articulate with the humerus. The distal part of the ulna did not articulate with the wrist. Comparison with the films taken in 1946 revealed no material change apart from a slight increase in the size of the bone and disappearance of several small radiolucent areas. The left radius and ulna were both of abnormal shape and size and contained radiolucent areas, mainly at the distal ends. The radius was shorter than the ulna, and the head of the radius did not articulate with the humerus. Both bones articulated poorly with the wrist. Apart from an increase in size, there was no material change from the 1946 films. The left femur was of normal shape and size for the patient's build. There was a radiolucent area running from the neck to the lower third, and small radiolucent areas were present in the condyles. There were some sclerosis and angling at the mid-shaft due to the old fracture. All the bones of both wrists were present, but were of abnormal shape. In the phalanges there were multiple enchondromata and ecchondromata involving most of the phalanges and metacarpals, slightly more pronounced on the right side. In most cases these chondromata were causing irregular expansion. Comparison with 1946 films revealed a slight increase in the lesions.

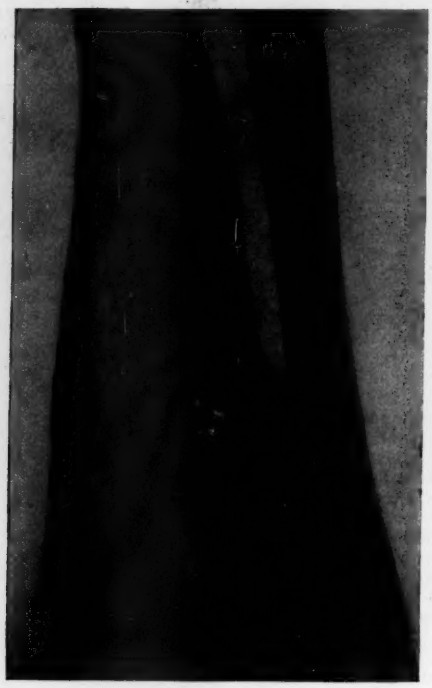

FIGURE VIII.

Skiagram of lower end of tibia, showing radiolucent areas with normal intervening bone running in a longitudinal direction.

The soft tissue changes found radiologically at the same time were as follows. Small soft-tissue tumours containing phleboliths were present in the left anterior triangle of the neck and above the left breast in the axillary line. Examina-

tion of the left wrist and hand revealed a soft-tissue tumour containing phleboliths in the region of the scaphoid—one at the base of the second metacarpal (not present in 1946 films), and another at the first metacarpo-phalangeal joint; this had increased in size since 1946. Examination of the right wrist and hand revealed a soft-tissue tumour containing numerous phleboliths in relation to the first metacarpo-phalangeal joint; this had increased in size since 1946.

Review of the 1946 films reveals soft-tissue tumours containing phleboliths in the right knee joints and in the region of both ankle joints.

The patient was considered to be suffering from Mafucci's syndrome of moderate degree.

FIGURE IX.
Skiagram of right ankle joint showing phleboliths in the soft-tissue tumours.

Discussion.

The pathogenesis of this condition is of considerable interest and somewhat in doubt. It is probably a mesodermal dysplasia arising at an early stage of fœtal life.

The linkage of two distinct conditions—the skeletal anomaly (Ollier's disease) and the hæmangiomata—is regarded by some authorities as coincidental; but the possibility remains that the vascular anomalies may determine the bone lesions. It is also possible that they are both consequent on a fœtal neurotropic disturbance.

Differential Diagnosis.

The differential diagnosis has to be made from the following conditions.

1. Neurofibromatosis (von Recklinghausen). This is not asymmetrical and occurs at a later age, and as a result there is no gross deformity. The tumours are pedunculated and pathologically distinctive. Radiological examination reveals saucer-shaped erosions on the outside of the bone, usually in association with an adjacent neurofibroma. Intraosseous cystic lesions may occur.

2. Polyostotic fibrous dysplasia (Albright's disease). In this condition fibrous dysplasia of the bone and multiple areas of skin pigmentation are associated with endocrine disorders such as sexual precocity in females, thyreoid disorders and acromegalic change. There are no subcutaneous tumours, and gross deformities do not occur. Radiological examination reveals numerous cyst-like areas in the bones, often bilateral, and commonly in the skull. If the cyst encroaches on the medullary border, a characteristic inner crescentic border is found.

3. Diaphysial aclasia (hereditary multiple exostosis). This is familial, and the cartilaginous growths occur on the surface of the bone.

Summary.

This case is reported as apparently the first case of Mafucci's syndrome recorded in Australia. As far as can be ascertained this is the twenty-fourth case reported in the literature.

The clinical and radiological features are described, and a brief reference is made to differential diagnosis.

Acknowledgements.

We wish to thank Dr. E. Dunlop and the Royal Melbourne Hospital for permission to publish details of this case, and to record the valuable help of the hospital photographer, Mr. R. Ingles, and of the Medical Division of Kodak, Australasia, Proprietary, Limited.

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OBSERVATIONS UPON THE EFFECTS OF "DIBENAMINE" IN MAN, WITH SPECIAL REFERENCE TO ITS ADRENOLYTIC AND NORADRENOLYTIC ACTION.

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AMONG the possible applications of an adrenolytic, or "adrenergic-blocking", agent is as a test for presence of a phæochromocytoma. This tumour is difficult to diagnose and, although rare, produces one of the few types of arterial hypertension which is susceptible to permanent relief by surgery. Until recently it has been believed that phæochromocytomata secrete adrenaline, but more recently Holton (1949) and other workers have found that they produce the closely related noradrenaline (Figure I), the pharmacological action of which differs in certain important respects from that of adrenaline (Goldenberg *et alii*, 1948; Barnett *et alii*, 1950).

The use of the adrenolytic agent "933 F", as recommended by Goldenberg and his co-workers (1947) in America, has been shown by Prunty and Swan (1950) in England and by myself (Barnett, 1950) to be unreliable as a test for circulating adrenaline and noradrenaline in man. In 1948 Spear and Griswold reported favourably on "Dibenamine" as a diagnostic agent in a case of phæochromocytoma, at a time when it was believed that these tumours secreted adrenaline. It was therefore thought appropriate to determine whether "Dibenamine" was an effective antagonist to both noradrenaline and adrenaline.

Brief Historical Review of the Use of "Dibenamine".

Introduction of "Dibenamine" and its Use in Animal Investigation.

N-N-dibenzyl-b-chloroethylamine (Figure I) was first produced by Eisleb (1934) and was later prepared in America by Givaudan-Delawanna Incorporated, under the name

"Dibenamine". Its activity as an adrenergic blocking agent was extensively studied by Nickerson and Goodman, who reported on its properties in 1947.

These workers and many others have continued to study this drug. In general it has been found to reverse most excitory effects of adrenaline, including the pressor effect, the pilomotor response and the production of cardiac irregularities in animals under cyclopropane anæsthesia, but not to abolish others, such as the cardiac acceleration and the increase in level of blood sugar. It has no effect on the inhibitory actions of adrenaline, such as the relaxation of certain types of smooth muscle. It is also effective in blocking the response to local sympathetic stimulation and the response to circulating "sympathin" (Nickerson and Goodman, 1947, 1948; Simeone and Sarnoff, 1947; de Vleeschhouwer, 1947).

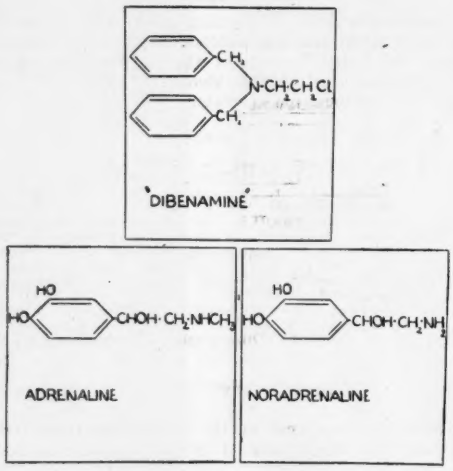

FIGURE I.

Structural formulæ of "Dibenamine", adrenaline and noradrenaline.

Evidence has been produced that "Dibenamine" blocks some essential step in the excitation process occurring between the arrival of the sympathomimetic agents at their site of action and the actual contraction of the smooth muscle cell (Nickerson and Nomaguchi, 1948).

With the development of knowledge of the effect of "Dibenamine" on recognized sympathetic activities, this drug has been used as a tool in the investigation of processes possibly related to sympathetic hyperfunction. Thus its action has been determined in cases of experimental hypertension (Nickerson and Goodman, 1948; Wilburne *et alii*, 1947; Nickerson *et alii*, 1948) and in traumatic and oligæmic shock (Remington *et alii*, 1948; Wiggers *et alii*, 1950).

The toxic properties of "Dibenamine" were realized early, and attention was drawn to them by Nickerson and Goodman (1947), who described the occurrence of local tissue damage and excitation of the central nervous system. Similar effects have been reported by other authors (Wilburne *et alii*, 1947; Sawyers *et alii*, 1947; Biörck, 1947).

The dosage of "Dibenamine" used in animal experiments was usually in the region of 10 to 40 milligrammes per kilogram of body weight, given by intravenous injection.

The Use of "Dibenamine" in Human Investigation.

In 1947 Hecht and Anderson reported on the first large series of patients to whom "Dibenamine" was given. They gave 62 injections to 36 patients. In general "Dibenamine" has the same effect in the human as in the experimental animal. Little change is produced in the resting normal subject. The effects of reflex stimulation of the sympathetic system, particularly on the vascular tree, but also on other organs, are blocked. The pressor effect of adrenaline is blocked, and adrenaline-induced cardiac irregularities are prevented, but certain other excitory effects, such as the tachycardia and increased circulatory rate, are not blocked. The inhibitory effects of adrenaline are not prevented.

As in animal experiments, so in human investigation, "Dibenamine" has been used as a tool in the elucidation of problems in normal and abnormal physiology. Thus Haemovici in 1948 observed that complete or partial inhibition of spontaneous sweating followed the administration of "Dibenamine", and deduced from this that there was evidence for an adrenergic component in the nervous mechanism of sweating in man. Haemovici and Medinets (1948) administered "Dibenamine" to a series of normotensive and hypertensive subjects and observed that in the normotensives there was no significant change in the resting arterial blood pressure. In cases of benign essential hypertension there was a significant fall in both the systolic and diastolic pressures, and in cases of malignant hypertension and of systolic hypertension associated with arteriosclerotic vascular disease there was no significant change.

The report by Spear and Griswold (1948) on the hypotensive effect of the administration of "Dibenamine" in a case of phæochromocytoma has already been mentioned.

Therapeutically, "Dibenamine" has been used in such widely separated fields as psychiatry and ophthalmology. Rockwell (1948) has reported benefit from its administration in patients in whom anxiety, fear, panic, resentment or anger were prominent features of their mental state. Christensen and Swan (1949) have reported that the administration of "Dibenamine" produces a fall in the intraocular pressure in cases of glaucoma.

Although the dose of "Dibenamine" given to humans (four to seven milligrammes per kilogram by slow intravenous injection) has been considerably less than that given to animals, toxic effects have been fairly commonly observed. Thus, Hecht and Anderson (1947) noted some toxic action in about two-thirds of the instances in which an injection of "Dibenamine" was given, and listed the following: nausea with or without vomiting, drowsiness and dizziness, sweating, nasal congestion and tingling of feet, restlessness, irritation and palpitation, pain along the arm during the infusion, thrombophlebitis, mental confusion and convulsions.

Other workers, such as Simeone and Sarnoff (1947), Haemovici and Medinets (1948) and Rockwell (1948), who have used the drug in a large series of patients, have recorded one or more of these unpleasant side effects. It has been stressed by the observers that they have been transitory.

Present Investigations.

The dose of "Dibenamine"[1] was weighed out on the day of the investigation and dissolved in a mixture of ethyl alcohol, propylene, glycol and hydrochloric acid,[2] and this was then added to about 500 millilitres of normal saline in a "Soluvac" flask. The dosage of "Dibenamine" ranged from 3·7 to 6·0 milligrammes per kilogram in any one case. The solution was given by slow intravenous drip administration over a period of about one hour and was preceded and followed by an infusion of saline.

In certain instances the "Dibenamine" was given during the course of an infusion of *l*-adrenaline or *dl*-noradrenaline, given at a rate such as to produce systolic hypertension (in the case of adrenaline) or systolic and diastolic

[1] The "Dibenamine" used in these investigations was a quantity of the hydrochloride obtained by Dr. P. Fantl, of the Baker Medical Research Institute, from Givaudan-Delawanna Incorporated.

[2] The "Dibenamine" was freshly prepared in a mixture with the constituents in the following proportions: 25 grammes of "Dibenamine" hydrochloride, 242 millilitres of alcohol (U.S.P. XIII), 242 millilitres of propylene glycol (N.F. VIII), one millilitre of hydrochloric acid (U.S.P. XIII). The mixture was slightly warmed until the crystals had gone into solution.

hypertension (in the case of noradrenaline), thus imitating the supposed mechanism of hypertension in cases of phæochromocytoma.

Effect of "Dibenamine" Alone.

In three subjects an infusion of "Dibenamine" was given without any concurrent infusion of adrenaline or noradrenaline. (In one of these cases short infusions of adrenaline and noradrenaline were given before and after the "Dibenamine" infusion.)

Individual doses were 3·7, 5·3 and 5·8 milligrammes of "Dibenamine" hydrochloride per kilogram of body weight administered over a period of about one hour. Although in two cases the blood pressures and pulse rate were somewhat unstable, in no case was there a fall during the "Dibenamine" infusion in the systolic or diastolic blood pressures to a level below those during a preliminary control saline infusion.

Effect of "Dibenamine" plus Adrenaline Compared with the Effect of Adrenaline Alone.

Four patients were given an infusion of *l*-adrenaline over a period of about one hour. In another four cases, during the infusion of *l*-adrenaline over a similar period, an infusion of "Dibenamine" was commenced about ten minutes after the adrenaline infusion started.

The response of the blood pressures and pulse rate during two experiments is illustrated in Figure II, one chart showing the effect of an infusion of adrenaline alone, the other that of adrenaline *plus* "Dibenamine".

Table I shows the average values for the blood pressures and pulse rate during the preliminary control period of saline infusion, during a fifteen-minute period commencing ten minutes after the start of the adrenaline infusion (by which time the latter had been adjusted to a constant rate), and during a fifteen-minute period ending at the conclusion of the adrenaline infusion or its change to a new rate. It also shows, in the three cases in which these observations were made, the response of the blood pressures and pulse rate to a much increased dosage of adrenaline. The data are shown diagrammatically in Figure III. It is to be noted that after the administration of "Dibenamine" the infusion of a dose of adrenaline larger than previously given failed to produce a further rise in the blood pressure, although in two cases there was an appreciable rise in the pulse rate. This is in accord with the observations made by others, that "Dibenamine" blocks the pressor effect of adrenaline, but not its action on the heart rate. In no case, however, did a reversal of the pressor action of adrenaline occur. The systolic blood pressure fell from the original hypertensive level produced by the adrenaline in all four subjects to whom "Dibenamine" was given concurrently with adrenaline, but there was also a fall in two of the four instances in which adrenaline was given alone. The diastolic blood pressure showed a further fall in three out of the four cases, and the pulse rate was higher at the end than in the early part of the adrenaline infusion in both series.

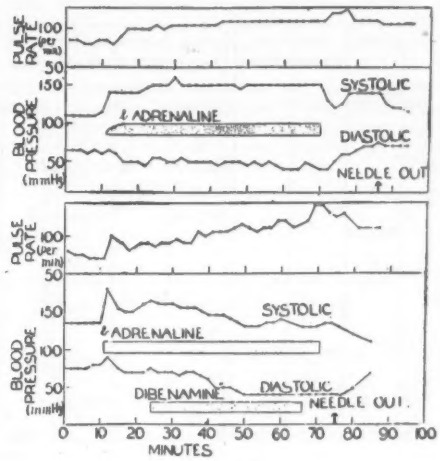

FIGURE II.

Effect on pulse rate, systolic and diastolic arterial blood pressures in two subjects from (*a*) infusion of *l*-adrenaline (above) and (*b*) infusion of *l*-adrenaline with addition of infusion of "Dibenamine" (below).

Effect of "Dibenamine" plus Noradrenaline Compared with the Effect of Noradrenaline Alone.

Four subjects were given infusions of *dl*-noradrenaline over periods ranging from seventy-seven to ninety-five minutes, and another four were given infusions of *dl*-noradrenaline over periods ranging from sixty-eight to eighty-eight minutes, with the addition of an infusion of

TABLE I.

Experimental Data: Infusion of l-Adrenaline and of l-Adrenaline plus "Dibenamine".

Subject.	Age in Yrs.	Control.			Infusion.									Adrenaline Dosage. (Micrograms per Kilogram per Minute.)		"Dibenamine" Dosage (Milligrammes per Kilogram.
					First Period.			Second Period.			Third Period.					
		Blood Pressure. (Millimetres of Mercury.)		Pulse Rate per Minute.	Blood Pressure. (Millimetres of Mercury.)		Pulse Rate per Minute.	Blood Pressure. (Millimetres of Mercury.)		Pulse Rate per Minute.	Blood Pressure. (Millimetres of Mercury.)		Pulse Rate per Minute.	First and Second Periods.	Third Period.	
		Systolic.	Diastolic.		Systolic.	Diastolic.		Systolic.	Diastolic.		Systolic.	Diastolic.				
B.McG.	29	123	64	101	147	52	117	148	49	138	—	—	—	0·48	—	—
A.T. ..	18	128	57	80	168	38	102	153	40	114	—	—	—	0·23	—	—
R.M.	23	120	73	77	158	44	111	144	20	123	—	—	—	0·29	—	—
J.McA.	37	111	63	83	151	51	104	149	43	109	—	—	—	0·46	—	—
P.D.	23	126	83	68	160	66	87	138	49	114	126	55	117	0·36	0·46	4·5
S.T.	23	117	67	77	158	63	101	121	50	116	123	50	160	0·22	0·71	4·1
F.O. ..	32	100	71	74	143	58	85	118	49	103	122	46	115	0·64	0·84	4·1
R.S. ..	24	135	76	74	159	69	89	133	40	123	—	—	—	0·21	—	4·4

Explanatory notes: Control = preliminary period of infusion with normal saline. First period = fifteen minutes commencing ten minutes after starting the *l*-adrenaline infusion. Second period = fifteen minutes ending at conclusion of *l*-adrenaline infusion or change to a higher rate. Third period = time during which the rate of the *l*-adrenaline infusion was greatly increased. The values recorded for the blood pressures and pulse rate during the control and first, second and third infusion periods are the averages of all the respective readings taken during these times. Dosage of adrenaline and "Dibenamine" are expressed in terms of the hydrochloride.

"Dibenamine" commenced after the noradrenaline effect on the blood pressures and pulse rate was established.

The responses of the blood pressures and pulse rate in two of the experiments are shown in Figure IV. Experimental data are summarized in Table II, which has been

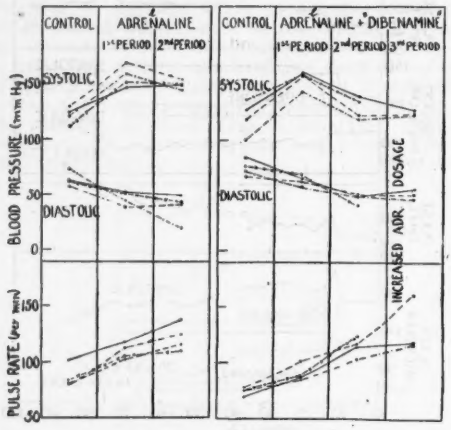

FIGURE III.

Diagrammatic representation of results in subjects receiving *l*-adrenaline and *l*-adrenaline *plus* "Dibenamine" infusions. The averages of all the readings of systolic and diastolic arterial blood pressures and the pulse rate during control and first, second and third infusion periods are represented as single points. "Control" = preliminary period of infusion with normal saline. "1st period" = fifteen minutes commencing ten minutes after start of the *l*-adrenaline infusion. "2nd period" = fifteen minutes ending at conclusion of *l*-adrenaline infusion or change to a higher rate. "3rd period" = time during which the rate of the *l*-adrenaline infusion was greatly increased.

constructed in a similar manner to Table I. The first fifteen-minute period is taken from a point twenty minutes after the commencement of the noradrenaline infusion, a longer time being taken in stabilizing the infusions at the desired constant rate than in the adrenaline experiments. Although the noradrenaline was administered as *dl*-noradrenaline-bitartrate monohydrate, for easy comparison, the dosage is expressed in the table as the amount of the active lævo form in an equimolecular weight of *l*-adrenaline hydrochloride. The data are shown diagrammatically in Figure V. It will be noted that in the two cases in which noradrenaline was given in a much

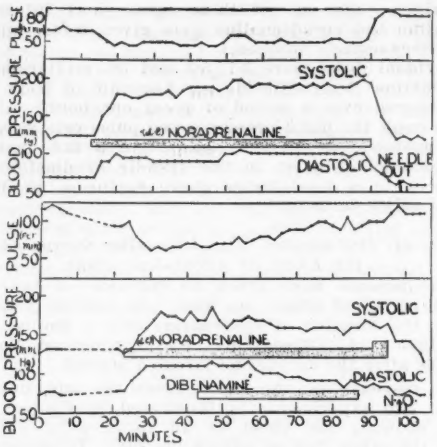

FIGURE IV.

Effect on pulse rate, systolic and diastolic arterial blood pressures in two subjects from (*a*) infusion of *dl*-noradrenaline (above) and (*b*) infusion of *dl*-noradrenaline with addition of infusion of "Dibenamine" (below).

increased dosage after the infusion of "Dibenamine" this failed to produce a rise in blood pressure, thus confirming the latter's noradrenolytic action. In only one of the four cases in which "Dibenamine" was given concurrently with noradrenaline was there an appreciable fall in the systolic blood pressure, but in all cases there was a pronounced fall in the diastolic blood pressure. However, an appreciable fall in the diastolic blood pressure occurred in two of the subjects given an infusion of noradrenaline alone, although in none of these was the decrease as great as in those to whom the "Dibenamine" was also administered. There was little change in the pulse rate at the end as compared with the early part of the infusion in those

TABLE II.

Experimental Data: Infusion of dl-*Noradrenaline and of* dl-*Noradrenaline plus "Dibenamine".*

Subject.	Age in Yrs.	Control.			Infusion.									Adrenaline Dosage. (Microgrammes per Kilogram per Minute.)		"Dibenamine" Dosage. (Milligrammes per Kilogram.
					First Period.			Second Period.			Third Period.					
		Blood Pressure. (Millimetres of Mercury.)		Pulse Rate per Minute.	Blood Pressure. (Millimetres of Mercury.)		Pulse Rate per Minute.	Blood Pressure. (Millimetres of Mercury.)		Pulse Rate per Minute.	Blood Pressure. (Millimetres of Mercury.)		Pulse Rate per Minute.	First and Second Periods.	Third Period.	
		Systolic.	Diastolic.		Systolic.	Diastolic.		Systolic.	Diastolic.		Systolic.	Diastolic.				
S.T.	23	112	48	71	163	66	51	166	54	54	—	—	—	0·25	—	—
F.W...	43	125	80	62	179	107	48	189	108	49	—	—	—	0·17	—	—
G.S. ..	20	132	71	83	170	94	62	170	82	60	—	—	—	0·29	—	—
J.D. ..	29	125	70	66	185	90	46	193	98	53	—	—	—	0·26	—	—
G.A.	20	129	73	109	172	111	70	159	86	96	163	79	100	0·29	0·54	6·2
P.D.	23	130	97	71	177	114	55	180	100	71	167	90	79	0·34	0·43	6·0
S.T.	23	116	74	74	168	94	51	169	76	66	—	—	—	0·29	—	4·8
W.H.	25	117	72	80	155	100	57	162	80	84	—	—	—	0·15	—	5·0

Explanatory notes: Control = preliminary period of infusion with normal saline. First period = fifteen minutes commencing twenty minutes after starting the *dl*-noradrenaline infusion. Second period = fifteen minutes ending at conclusion of *dl*-noradrenaline infusion or change to a higher rate. The values recorded for the blood pressure and pulse rate for the control and first, second and third infusion periods are the averages of all the readings taken during these times. In statement of the dosage of noradrenaline only the actine (lævo) component is considered, and this is then expressed in terms of equimolecular weights of adrenaline hydrochloride. The "Dibenamine" dosage is expressed in terms of the hydrochloride.

given noradrenaline alone, whereas in all four subjects to whom "Dibenamine" was also administered there was an increase in the pulse rate at the end of the infusion.

In one subject an attempt was made to determine the length of the adrenolytic and noradrenolytic activity of "Dibenamine", and the results are shown in condensed form in Figure VI. The resting blood pressures were found to be steady over a control period of ninety minutes. The effect of an infusion of *l*-adrenaline and *dl*-noradrenaline was observed. During a subsequent infusion of "Dibenamine" (5·3 milligrammes per kilogram over a period of fifty-three minutes) the blood pressures remained substantially unchanged. An infusion of noradrenaline immediately following that of "Dibenamine" produced much less rise in the systolic blood pressure than

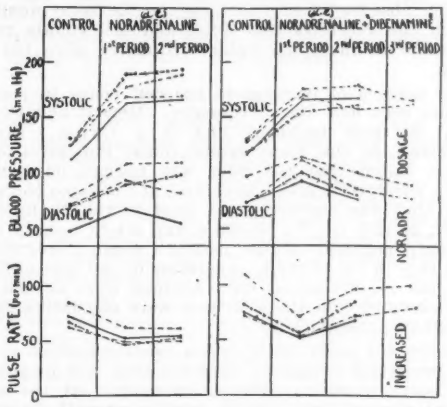

FIGURE V.

Diagrammatic representation of results in subjects receiving *dl*-noradrenaline and *dl*-noradrenaline *plus* "Dibenamine" infusions. The averages of the systolic and diastolic arterial blood pressure readings and pulse during the control and first, second and third infusion periods are represented as single points. "Control" = preliminary period of infusion with normal saline. "1st period" = fifteen minutes commencing twenty minutes after start of *dl*-noradrenaline infusion. "2nd period" = fifteen minutes ending at conclusion of the *dl*-noradrenaline infusion or change to a higher rate. "3rd period" = time during which the rate of the *dl*-noradrenaline infusion was greatly increased.

previously, and no change in the diastolic blood pressure; an infusion of adrenaline produced a slight fall in both the systolic and diastolic blood pressures. Twenty-four hours later an infusion of noradrenaline still produced a greatly diminished response, and an infusion of adrenaline produced a slight rise in the systolic and fall in the diastolic blood pressure. After forty-eight hours the response to infusion of noradrenaline had returned to almost its pre-"Dibenamine" value, but there was still some modification of the response to adrenaline.

The presence of postural hypotension following a "Dibenamine" infusion was tested for in only four cases; it was found to be absent in one, slight in two and pronounced in one.

The skin sensitivity to the injection of five minims of solutions of *l*-adrenaline hydrochloride and of *dl*-noradrenaline bitartrate monohydrate in concentrations of 1 in 1000 and 1 in 10,000 before and after an infusion of "Dibenamine" was tested in three cases. The area of blanching was less after the infusion of "Dibenamine", but was not abolished. The decrease in the pilomotor response was greater than that of the blanching.

Toxic Effects.

Nasal congestion occurred in practically all cases, but gave no cause for complaint. Nausea with or without vomiting occurred three times. One patient reported later that he had slight mental confusion towards the end of the infusion, time seeming to stand still and the same thought going through his mind many times. One patient had a more pronounced toxic psychosis lasting about one hour, again characterized by countless repetition of the one thought and disorientation in time. Localized venothrombosis at the site of the infusion occurred in one instance.

Summary and Conclusions.

In order to determine the value of "Dibenamine" in a test for the presence of a phæochromocytoma, the effect of this drug on the hypertension produced by adrenaline and noradrenaline (the substances believed to be secreted by this tumour) was investigated.

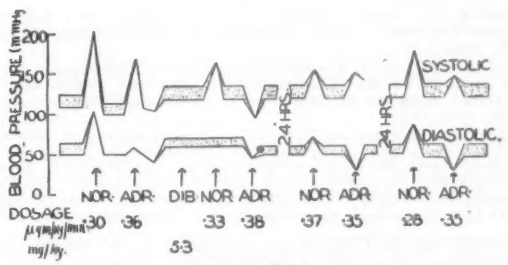

FIGURE VI.

Representation in a condensed form of the results in an investigation in one subject of the modification of the pressor effect of adrenaline and noradrenaline by "Dibenamine". The thick lines on the chart include all the readings for the period represented. Peaks denote highest or lowest readings. Gaps indicate periods in which records were not made or were incomplete. Time not to scale. The adrenaline used was the *l*-adrenaline hydrochloride and the noradrenaline *dl*-noradrenaline bitartrate monohydrate, but, for easy comparison, doses have been expressed in terms of equimolecular quantities of *l*-adrenaline hydrochloride.

"Dibenamine" hydrochloride was administered by slow intravenous infusion to 11 subjects in doses ranging from 3·7 to 6·2 milligrammes per kilogram.

"Dibenamine" alone produced no significant changes in the systolic or diastolic blood pressure or in the pulse rate.

When administered after an infusion of "Dibenamine", an infusion of *dl*-noradrenaline produced only a slight rise in the systolic and no change in the diastolic blood pressure (instead of the usual pronounced rise in both these pressures), and an infusion of *l*-adrenaline produced a fall in the systolic and diastolic blood pressure (instead of the usual rise in the systolic with no change or fall in the diastolic blood pressure).

When "Dibenamine" was administered during the course of an adrenaline infusion, the systolic blood pressure fell from the hypertensive level produced by the adrenaline.

When "Dibenamine" was administered during the course of a noradrenaline infusion, the diastolic blood pressure fell from the hypertensive level produced by the noradrenaline.

However, in the time taken for these latter two effects to occur, in certain subjects given infusions of adrenaline and noradrenaline without "Dibenamine", there was a fall in these blood pressures from the early hypertensive levels. Because of this, the use of "Dibenamine" as a diagnostic agent in cases of suspected phæochromocytomata is of limited value.

"Dibenamine" has certain toxic actions which limit its use in human investigation.

Acknowledgements.

Grateful acknowledgement is made to Dr. T. E. Lowe for helpful advice and encouragement, to Dr. P. Fanti (Baker Medical Research Institute) for the supply of

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A CLINICAL DESCRIPTION OF A DISEASE RESEMBLING POLIOMYELITIS, SEEN IN ADELAIDE, 1949–1951.

By R. A. A. PELLEW,
Adelaide.

AN epidemic of poliomyelitis broke out in Adelaide in May, 1949. The number of patients admitted to the infectious diseases wards at Northfield increased as the epidemic became more serious. Most of these early cases were severe paralytic poliomyelitis, with cerebro-spinal fluid cell counts varying round 50 per cubic millimetre. However, in August of that year a very unusual disease began to be seen. One of its most outstanding features was the absence of any increase in the total number of cells in the cerebro-spinal fluid, and cell counts ranging from none to three per cubic millimetre were the usual finding.

This absence of increase in the cell count in poliomyelitis has been described frequently. Merritt and Fremont-Smith in their text-book call it a rarity. However, Horstmann, at the First International Poliomyelitis Conference, stated that the fluid was normal on occasions, even in paralytic stages. Anderson, at the same conference, stated that the cerebro-spinal fluid might be normal in as high as 12% to 15% of cases, and might remain normal even until paralysis or the patient's death. Mugrage also stated that in 7% of cases, regardless of the type of involvement, the cerebro-spinal fluid findings were normal. But it is presumed that these writers were discussing cases of "classical" poliomyelitis.

The present paper deals with a condition which in many ways resembles "classical" poliomyelitis, but in a host of other ways is vastly different from it. At the present moment[1] the epidemic is still continuing with its mixture of this unusual type and "classical" poliomyelitis.

Of 1350 consecutive patients admitted to hospital, approximately 800 had less than 10 cells per cubic millimetre in the cerebro-spinal fluid, and of these 800, by far the majority had less than five cells per cubic millimetre. These figures are being worked out in detail at present.

Age.

About one-fifth of all patients were in the five to nine years age group. Those under the age of five years accounted for approximately 15%. The age groups of ten to fifteen, fifteen to twenty, twenty to twenty-five, and twenty-five to thirty years accounted for about 10% each. A gradual decline in each decade was seen after the age of thirty years. There were no patients older than sixty-five years.

Clinical Description.

The onset of the disease may be either insidious or abrupt. Many patients said that they had been feeling vaguely off colour for perhaps three months, with occasional bouts of headache, associated with lassitude and aches in limbs, lasting for two days or so. Before their admission to hospital there was the usual story of increasing malaise and headache.

Some, however, developed sudden headache. The feature of the headache was outstanding, an almost constant symptom being that the headache was the worst ever experienced. It was usually "bursting" in type and generalized, although in some cases occipital, lasting from one to seven days. A common symptom was pain behind the eyes, with much discomfort on moving the eyes from side to side. Upper respiratory tract infection was usual, there being sore throat, although some patients were admitted to hospital with frank pneumonia. Aching of limbs was a constant feature, worse in the legs, with occasional hyperæsthesia. Before admission to hospital vomiting and diarrhœa sometimes occurred; the latter was followed by obstinate constipation.

[1] April, 1951.

Difficulty in commencing the act of micturition was an irritating symptom, necessitating catheterization on occasions. The range of temperature was from just above normal to 102° F., the average being just under 100° F., and the duration of fever, with fall by lysis, was short, about three days being usual.

Stiff neck and stiff back were constant, both as symptoms and as signs, the tripod sign being very much in evidence. The back rigidity was greater than the neck rigidity, and often lasted as long as ten days.

One patient when admitted to hospital had a slightly stiff back, which became very stiff in three days' time; the stiffness lasted in all for nineteen days.

Cranial nerve lesions were consistently few, an occasional facial lesion being seen. Nystagmus was not common, but when seen exhibited some interesting features in its variability. A patient examined in the morning might have nystagmus, which would disappear at midday, recur later, disappear later and recur next day.

Muscle Weakness.

Generally muscle weakness was not very severe. Diffuse slight muscle weakness was the outstanding feature. It was much more common in legs than in arms, and very frequently affected *tibialis anticus* and *gluteus medius*. In by far the majority of cases the weakness was so mild as to be disregarded. If weakness was present, frequently it disappeared rapidly. This was especially so in those patients stricken with early severe paralysis. One such case in particular was of interest.

A man from the country, feeling vaguely "off colour" one day, developed a headache next day, and on the following day gave the history that it was necessary for him to be lifted off his motor-cycle owing to loss of muscle power. He was admitted to hospital that day with almost complete paralysis of his right arm, and almost complete paraplegia, there being some movement in his right great toe. Intense hyperæsthesia was also present in this case—so much so that stroking the skin with cotton wool caused agonizing pain. Muscle recovery was rapid for the first week or so, and slow but sure for the next two months. Eventually he was discharged from hospital with no disability.

Some patients still had weakness some three months or so after the onset, but for the most part the prognosis as to muscle weakness has been good.

There have been two rather unusual features concerning muscles, the first being very common and the second not uncommon. Almost every patient has complained of pain in various muscles for the ensuing six months. This pain has been severe, necessitating on occasions rest in bed, and not responding very well to salicylates or codeine. This pain has naturally hampered the after-treatment by reeducation, and has been the cause of a great deal of wastage of manpower. The second unusual feature has been experienced by many a practitioner in Adelaide. A patient may report with or without a history of an illness characterized by headache, malaise and fever. Perhaps some three months after such an illness the patient has suddenly discovered he has some muscle weakness. In fact, in a follow-up of 50 of these patients known to have had this unusual disease many had no weakness two months after the original onset, but had real weakness of isolated muscles a month or so later.

Cerebro-spinal Fluid Findings.

No abnormality in the cerebro-spinal fluid was found almost constantly in these cases. Fifty-nine consecutive patients were subjected to lumbar puncture on the day of their admission to hospital, and this puncture was repeated in seven days. All had less than five cells per cubic millimetre in the cerebro-spinal fluid, the number in the majority of cases being none to three cells on the first occasion. Fluid from five patients on the second puncture was found to contain more than five cells per cubic millimetre, the range being 44 to 88, but in the remainder of cases the fluid had a cell count range of none to five per cubic millimetre. The protein content was consistently normal at both punctures; in only two cases did it rise above normal at the second puncture (45 and 60 milligrammes *per centum*). All other investigations on the fluid gave normal results. The pressure was not raised.

Course.

The duration of fever and symptoms was short-lived. In about five days the patient looked and felt much better. But one most interesting observation was the frequency with which the temperature would rise on the seventh to tenth day, perhaps merely to 99·6° F., with a recurrence of headache, lassitude, malaise and muscle pain. This was not considered to be connected in any way with the second lumbar puncture, because it occurred in patients whose lumbar puncture was not repeated. This recurrence of symptoms lasted for about two days only.

Sequelæ.

In the sequelæ lies the greatest disability of this condition. One refers to the psychological phenomena which have complicated this disease so consistently. After the initial active stage the patient feels well, but in a period varying from four to eight weeks he experiences a lack of concentration, which has kept many away from work, together with a most intense depression. This latter state has not responded to any treatment and has lasted in some cases up to six months.

Irritability and emotional instability have always been most apparent, in many cases with hyperacuity of hearing. This last-mentioned symptom has been possibly a part of irritability and emotional instability, but it has been volunteered as a symptom by many patients.

Lassitude has been a natural corollary of these symptoms. Many patients have complained of difficulty of accommodation with blurring of vision. On examination no error of refraction has been discovered.

A good example of the sequelæ of this condition can be given.

Two men were admitttd to hospital about the same time; one had "classical" poliomyelitis, with 86 cells per cubic millimetre in his cerebro-spinal fluid and much muscle weakness in his legs; the other, mentioned previously, was almost paraplegic, except for some movement in his right great toe, and he had gross weakness of his right arm; this patient's cerebro-spinal fluid contained three cells per cubic millimetre. The patients were examined frequently, but at two months' interval their condition was reviewed. The former had made no recovery of any note in his muscle power, but was the most cheerful patient in the ward. The latter had recovered all his muscle power, but was extremely irritable and almost melancholic.

Another sequel has been observed. During the recent hot weather in Adelaide many patients have reported with headache, malaise, stiff neck, stiff back, fever and aches and pains in limbs, complaining that they have had another attack of poliomyelitis. When examined they exhibit the signs and symptoms of this peculiar condition in the same way as they did when originally attacked. The duration of this recurrence has usually been short, but one has seen one patient have as many as five such recurrences of symptoms. Sweating, which has been a pronounced feature of the condition in all stages, has also continued for some months. It has been mostly seen in the hands, although it has been present in other parts of the body. It has been rather an unpleasant sequel.

Mortality.

There have been no deaths from this disease.

Prognosis.

The prognosis is universally good, as regards both muscle power and psychological sequelæ. Those patients who have rapidly improved muscle power have had shorter illnesses. The psychological sequelæ have been prolonged in some people, but have nevertheless resolved eventually. The recurrences of symptoms which have taken place in some cases have tended to be less severe on each occasion.

Treatment.

The treatment carried out has been that of classical poliomyelitis. Rest has been essential during the acute stage and in some cases has had to be prolonged, mainly because of muscle aching. If aching has occurred, the only method possible has been rest, with the administration of some salicylates and codeine. In the absence of aching muscles reeducation has been carried out with satisfactory results. The opinion has been formed that, in the absence of muscle pain, energetic muscle movement is more satisfactory.

Deformities have been corrected by appliances. Pethidine has been found useful in the acute stages for the relief of pain and headache. Morphine is contraindicated owing to its depressant effect on the respiration. Constipation has necessitated glycerin and oil or magnesium sulphate and glycerin enemata.

The most satisfactory treatment of the psychological phenomena has been with reassurance backed by tonics.

Conclusion.

A description of a disease resembling poliomyelitis has been given. In many ways, especially in the early stages, the clinical picture is indistinguishable from that of poliomyelitis. The condition has differed from poliomyelitis in the constant absence of any increase in the cell count of the cerebro-spinal fluid, in the relatively rapid improvement in muscle power, and in the presence of psychological complications. The last-mentioned have been perhaps the outstanding features of the condition and have shown themselves as depression, emotional instability, irritability, lack of concentration and hyperacuity of hearing. There has been some upset of accommodation, causing blurring of vision in many cases. Some patients have been pronounced to have no muscle weakness, but after an interval of about three months muscle weakness has shown up.

Burnet has pointed out that poliomyelitis has tended to change its characteristics over the last decade or so. This condition, in the early stages, has been clinically indistinguishable from poliomyelitis. It is therefore possible that this condition is a mutational form of poliomyelitis. Virus investigation is at present being carried out by the University of Adelaide, under the auspices of the South Australian Government, in an attempt to isolate the organism.

Reviews.

CYTOLOGY OF THE VAGINA.

"CYTOLOGY OF THE HUMAN VAGINA", by two Spanish writers, Inés L. C. De Allende and Oscar Orías from the Mercedes and Martin Ferreyra Institute of Medical Investigation, Cordoba, Argentina, has a foreword by Bernard Houssay and has been translated from the Spanish by George W. Corner, Baltimore.[1] Dr. De Allende studied under Ephraim Shorr, of the Cornell University Medical School in New York City, and Carl G. Hartman and George Corner in Baltimore, at the Department of Embryology of the Carnegie Institution of Washington. Dr. De Allende than returned to Cordoba and she and her fellow author have now published the results of studies made over a period of five years.

The present monograph summarizes long-term studies on vaginal cytology made during those five years on some 200 women and including both normal and abnormal subjects. Their objectives are four in number: firstly, to demonstrate the great utility and easy application of the vaginal smear studies with the Shorr trichrome stain and of the resulting cytologic graphs; secondly, to describe the normal vaginal cycle as an indication of ovarian function; thirdly, to describe some of the functional anomalies of the female cycle; and lastly, to furnish a guide to the procedures and interpretations for those who wish to carry out for themselves the study of vaginal smears.

The authors have described the vaginal epithelium at the various phases of the menstrual cycle in some detail, and have included illustrations of actual biopsies of vaginal epithelium. Particular attention is given to the preparation of the vaginal smear, and the authors' method differs from that advocated by the majority of workers. They state that the smear when collected in the glass pipette must not be spread onto the slide by the curve of the pipette, but should be blown onto the slide and on no account be disturbed. Their argument is that at certain times the actual clumping of the squamous cells may be of considerable importance.

The technique of staining the smears is thoroughly discussed and a description of the cells encountered in the vaginal smear is given, the term "deep" cell being used in place of the more commonly used basal cell.

Cytological graphs are used extensively to illustrate the proportion of each of the different cellular elements in the smear and to indicate the state of development of the vaginal epithelium. The minimum number of cells to be counted on each occasion is 400, and as daily counts are made on a number of patients, this method, whilst no doubt having certain advantages, must also be unusually time-consuming. A detailed description of the curves is given; that characteristic of the normal menstrual cycle is the "euthropic" curve, in which the number of cornified cells rises to a maximum of 90% near the middle of the cycle; the "cyclic hypotrophic" curve resembles the "eutrophic" curve in general shape, but the percentage of cornified cells remains below that of the latter. The "non-cyclic hypotrophic" curve shows very low percentage of cornified cells and remains lower throughout the cycle, whilst the "curve of persistently high cornification" may show a high percentage of cornified cells extending over many months. The authors have used this cytological method to illustrate the changes that can be detected in the vaginal epithelium in anovulatory cycles, in functional amenorrhœa, at the menopause, in *metropathica hæmorrhagica*, in cases of sterility and following bilateral oophorectomy. In particular this method has been used to follow the action of hormones on the ovary which reflect profound changes in the vaginal epithelium.

The work of the authors has been most painstakingly performed, though it would appear that in some of the sections the number of cases is very small.

The book is well illustrated with 23 coloured plates and 52 other illustrations, the majority of which are cytological curves.

[1] "Cytology of the Human Vagina", by Inés L. C. De Allende, M.D., and Oscar Orías, M.D., with a foreword by Bernardo A. Houssay, M.D., and translated from the Spanish by George W. Corner, M.D.; 1950. New York: Paul B. Hoeber, Incorporated. 9¼" × 6", pp. 316, with many illustrations, some of them coloured. Price: $7.50.

WOMAN THROUGH THE AGES.

DR. HARVEY GRAHAM, the author of "Surgeons All", has written an important book, "Eternal Eve".[1] It is described on the jacket as "The Story of Women from the Stone Age until Today". Eternal Eve is named by the author as the mythical "Mother of All Living". He states in his preface that the story ranges widely. "It has moments of tragedy, moments of great excitement, and a mingling of art, science, and humanity. Major tragedies and minor ribaldries form a background for great men and outstanding women. Rubbing shoulders with them are midwives and charlatans, man-midwives and quacks." The book is intended for the ordinary man and woman ("a group that includes doctors and medical students"); "it is essentially a story book". It should be stated at once that the author covers his extensive field with an amazing wealth of information—he has produced what may be compared with an enormous painting, not in the manner of the impressionists but with a careful attention to detail. The result is that the reader must proceed with care; indeed, he may find that one reading of a chapter is not enough. The second reading will be worth while. The author must have got a good deal of pleasure out of his writing; his sense of humour is reflected by the way in which he introduces some of the incidental anecdotes and by his occasional comments on them.

The story begins with the time when midwifery began and is carried on to the present day. A typical legend of the beginning of midwifery comes from the Dyaks of Borneo. Kelili, whose wife Teburi was big with child, went into the jungle seeking food. He came to the place of the big monkeys and saw what he had never seen before—a

[1] "Eternal Eve", by Harvey Graham; 1950. London: William Heinemann (Medical Books), Limited. 10" × 6", pp. 726, with many illustrations. Price: 42s.

young female with a great belly calling out with pain. She crouched on the ground and her mate waited beside her. Kelili waited and watched and learned how husbands among the big monkeys helped their wives at the birth of their young. He remembered, and when the birth pains came to Teburi he helped her, doing what he had seen the monkey husband do. From this Harvey Graham traces the development of the obstetric art and the many duties of the midwife. In Rome midwives extended their activities to matchmaking, and often they had to attest virginity and later to confirm consummation; some of them apparently were sufficiently skilled to undertake minor gynæcological manœuvres. The author has a good deal to say about Soranus who came to Rome in A.D. 98 and died about A.D. 138. His work was "easily the most important of ancient times" and it continued to be important for 1500 years. If there were any obstetricians of the calibre of Soranus for 1400 years after his death, everything that they wrote or did is lost. No real additions were made to obstetrics until the days of Ambroise Paré, who revived the practice of podalic version which Soranus had been the first to describe. Paré lived from 1510 to 1590. Then we read of Vesalius, Fallopius, Eustachius and Arantius. After this comes William Harvey, the discoverer of the circulation, who, because of the chapter *"De Partu"* in his book *"De Generatione Animalium"*, was designated by Aveling as the Father of English Midwifery. William Smellie advanced the art and taught many pupils. He was a man of resource—when he chanced to divide an infant's umbilical cord on the wrong side of the ligature he explained solemnly to the midwife, when he had checked the bleeding, that this was his new way of preventing convulsions in the infant. William Hunter stands out as being the first in Great Britain to apply enlightened methods of teaching and investigation to anatomy and particularly to the anatomy of obstetrics. It is impossible to name all the men who stand out in this story. Mention must, however, be made of Charles White, "Man-Midwife Extraordinary", who made the first essay in preventive obstetrics on the lines of general hygiene. Later of course we come to Semmelweis and then to Pasteur and Lister and Röntgen and the moderns.

To describe this book adequately much more space would be needed. The evolution of the man-midwife and the setting up of standards in obstetrical education and practice have not been referred to; nor has mention been made here of Cæsarean section and obstetrical forceps. The story of forceps and especially of the Chamberlens with their "secret" which they guarded successfully for several generations, is worth the telling. Superstition takes a large place in human life and in pregnancy and obstetrics is rife to this day, as most general practitioners can testify. Ideas on some matters do not seem to have altered. We read that in Germany in the Middle Ages redheads were not popular in the wet-nursing business and that brunettes were thought to be more reliable that blondes. Women went to great lengths in olden times to preserve their beauty. Early in the seventeenth century a Hungarian countess was much criticized for bathing in fresh young blood to preserve her fading charms. "Nobody doubted the efficacy of the method, but her slaughter of twenty-four virgins in order to fill her blood-bath to overflowing was regarded as unduly extravagant." Virgins have always had value in the eyes of the superstitious and the author states that at one time Mary Baker Eddy went so far as to enlist a guard of virgins to protect her from certain malign forms of animal magnetism.

Harvey Graham's "story" can be commended to the attention of medical men and women; non-medical persons who have a literary bent or are historically minded and those who are interested in humanity as such will derive pleasure from it. Medical folk must not imagine that it is a text-book. It is not intended to be. It is a story, left purposely without footnotes. For all that it is something which every gynæcologist and obstetrician should read with care.

PHYSICAL MEDICINE.

THE scope of physical medicine has broadened greatly in the past decade, and "Recent Advances in Physical Medicine" by Francis Bach presents the modern ideas upon this comparatively new specialty.[1] Chapters are contributed by various authors, each of whom is an acknowledged specialist in the particular subject. The use of physical therapy in such specialties as plastic surgery, dermatology and pædiatrics is dealt with and treatment is discussed from all angles in a general manner, but the book would be of greater value to practising doctors and physiotherapists had the finer details of treatment been enumerated more completely.

Occupational therapy and rehabilitation in industry are included as well as details for the organization of a physical medicine department. The rheumatic diseases occupy some 24 pages, but it is perhaps surprising to find little mention of spondylitis and no mention of sinusitis, both maladies in which physical therapy can be used advantageously, but, as stated on the cover, "of necessity some omissions are acknowledged". If this is through shortage of paper, it is to be hoped that the work will be enlarged to allow the inclusion of all the omissions when it is reprinted.

[1] "Recent Advances in Physical Medicine", edited by Francis Bach, M.A., D.M. (Oxford), D.Phys.Med.; 1950. London: J. and A. Churchill, Limited. 8″ × 5½″, pp. 512, with 93 illustrations. Price: 27s. 6d.

INJURIES TO THE ANKLE.

"INJURIES TO THE ANKLE", by Dr. J. Grant Bonnin, is a veritable encyclopædia of the subject in question, and should be the complete book of reference for many years to come.[1]

This book should prove of inestimable value to those concerned in the training of students, to those doing post-graduate study in traumatic surgery, and to radiologists. Undergraduates in medicine will find the subject matter too protracted for such a small portion of their course.

Mr. Bonnin must be congratulated on the amount of research, both literary and clinical, reflected in this publication. The 399 illustrations, mostly X-ray prints, are of excellent quality, and an extensive bibliography is appended. The book contains a lengthy historical survey of the subject, a chapter on the detailed anatomy of the parts involved, very useful sections on the radiography of the ankle joint, and the mechanisms of the various fractures. The remainder of the book is devoted to the individual lesions, surgical approaches to the ankle, and the late results and complications of injuries of the ankle. Radiologists will find many points to interest them in this book.

The only criticisms one can offer are with regard to the number of words used and a rather unnecessary amount of repetition in various chapters of the book. Mr. Bonnin would render a great service to practising surgeons by publishing a small edition embodying the salient features and X-ray prints of the present edition.

TUBERCULOSIS AND OTHER PROBLEMS OF PÆDIATRICS.

IT would be difficult to imagine an easier to read and more informative production than the small volume published under the title "Tuberculosis and Other Problems of Pediatrics" by Arvid Wallgren, M.D.[2] This work constitutes Series Number Ten of the Abraham Flexner Lectures.

The idea of these lectures is an excellent one; they were founded by Mr. Bernard Flexner to commemorate the wonderful work done by Abraham Flexner for the development of the Vanderbilt Medical School. This is all the more remarkable when it is recalled that Abraham Flexner, as is not generally known, was not himself a physician. An essential condition is that the lecturer stays for a period of two months and joins in the educational, clinical and scientific work of the Medical School.

The first subject dealt with is "General Trends in Combating Tuberculosis in Childhood" and emphasis is placed upon prevention and treatment. It is made clear that there is in the long run a self-regulating factor in the incidence of tuberculosis with a pronounced tendency to diminish the morbidity and mortality rates. This happens, however, solely under normal conditions and the trend is jeopardized by war, famine and other abnormalities, alas so frequent in Europe during this century.

The rationale and practical details of B.C.G. vaccination are very clearly set out for the busy reader.

[1] "Injuries to the Ankle", by J. Grant Bonnin, M.B., B.S. (Melbourne), F.R.C.S.; 1950. London: William Heinemann (Medical Books), Limited. 8½″ × 5½″, pp. 432, with many illustrations. Price: 63s.

[2] "Tuberculosis and Other Problems of Pediatrics: The Abraham Flexner Lectures Series Number Ten", by A. Wallgren, M.D.; 1950. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 8″ × 5″, pp. 132, with illustrations. Price: 24s. 3d.

The chapter on *erythema nodosum* is most informative, and Wallgren regards this manifestation as a non-specific cutaneous eruption which appears especially in tuberculous and occasionally in other infections, and may possibly be provoked by non-infectious agents. It may serve as a diagnostic agent for the detection of a fresh tuberculous infection, and may be of great value in revealing the source of infection. In a tuberculin-positive individual it nearly always indicates that the tuberculous infection occurred three to eight weeks previously.

The next chapter dealing with the illegitimate child in Sweden indicates the efficient measures taken in that country to deal with this ever-present problem, the aim being to ensure as far as possible the same rights and the same chances of life and health, development and education to all children whether legitimate or illegitimate.

The concluding chapter on infantile hypertrophic stenosis of the pylorus is a fascinating one, especially stressing the Röntgen-anatomical studies which demonstrate that the anatomical condition can persist even for some years after the clinical manifestations have subsided. Two other important observations are the occurrence of splenomegaly and hypoprothrombinæmia in infants suffering from this condition.

The volume is well printed, and there is an adequate bibliography at the conclusion of each chapter. These essays merit a place in every pædiatric library.

TUMOURS OF THE HEAD AND NECK.

DR. GRANT E. WARD AND DR. JAMES W. HENDRICK have rendered a very useful service by collecting into one volume a great deal of authoritative information on tumours of the head and neck.[1] This is an area of the human body where several specialists have their interests side by side. For the most part they can practise in their chosen field without worrying too much about the intricacies, developments or problems in the realms of other specialists. But tumours, particularly malignant tumours, do not recognize the artificial boundaries drawn by man. It is therefore useful to have an account of tumours in this region collected into one volume instead of having to consult text-books of dermatology, ophthalmology, surgery, rhinolaryngology and so on, particularly for those growths which overlap the conventional boundaries.

The authors have based the book on many years of experience, mainly in the University of Maryland Hospital and the Johns Hopkins Hospital. As the authors state in their preface, the book is written essentially for the clinician; it is intended to help in the early diagnosis and the choice of correct treatment of tumours of the head and neck. These objects have been admirably achieved. Many of these tumours cross the boundaries of two or more of the commonly recognized specialties, and the authors rightly insist that often, in such cases, a team management of the problem may serve the patient's interest best. As an earnest of this team spirit they have called upon various colleagues to write parts of the book which deal with more highly specialized and restricted fields. The names of these contributors appear at the head of the chapter or section which each contributes.

Although it would be impossible to give the best method of treatment for every tumour readers are likely to encounter, the authors give so many examples from their own practice that it would be a rare problem indeed if, at least, some guiding principles for its solution could not be found in this book. In a decision on the best method of treating a tumour a warning is given against slavish adherence to radiation, to electro-surgery or to excision. Each case must be judged on its own merits. Indications are given as to which method or which combination of methods of attack must be employed. The method or methods of choice are fully discussed for each kind of tumour and many a pitfall is pointed out. Descriptions of both the gross and microscopic pathological changes are given in sufficient detail to enable the clinician to understand the nature of the tumour afflicting his patient. But the pathologist faced with the problem of diagnosis of a rare tumour or unusual variations of tumours will have to consult monographs or larger works devoted to pathology.

[1] "Diagnosis and Treatment of Tumors of the Head and Neck (Not Including the Central Nervous System)", by G. E. Ward, M.D., D.Sc., F.A.C.S., and J. W. Hendrick, M.D., M.S.; 1950. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10" × 6¾", pp. 852, with many illustrations, some of them coloured. Price: £8 1s. 9d.

The book is liberally illustrated in both black and white and colour. The photographs of clinical features and the photomicrographs are of a high order of clarity, and so are the hand-drawn illustrations. There is a tendency these days to rely too much upon photography to illustrate a book. It is pleasing to note that the authors of this volume have used line diagrams or hand-drawn illustrations in preference to photographs whenever these have been more appropriate to elucidate the points they wish to make, particularly in reference to anatomy and surgical procedures.

The book is written in twenty-one chapters. A chapter on the embryology of the head and neck follows a short introductory chapter. Then the benign and premalignant conditions, followed by the malignant tumours of the different parts—skin, lips, oral cavity, jaws, salivary tissue, tonsils and pharynx, nose and nasal cavities, eye, ear, larynx—primary tumours of the neck (including thyreoid), tumours of lymphoid tissue, metastatic tumours and tumours of the skull are each given one or more chapters. The last chapter, "Rehabilitation", is devoted to reconstructive surgery for the repair of defects left in the bony or soft tissues after a growth has been eradicated.

Tumours of the central nervous system have been omitted by design.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"A Complete Outline of Fractures including Fractures of the Skull for Students and Practitioners", by J. Grant Bonnin, M.B., B.S. (Melbourne), F.R.C.S. (England); Third Edition; 1951. London: William Heinemann (Medical Books), Limited. 8¾" × 6", pp. 686, with 710 illustrations. Price: 42s.

Intended for the "undergraduate and the post-graduate student".

"Personality and Psychosis", by Otho W. S. Fitzgerald, M.A., M.D. (Dublin); 1951. London: Baillière, Tindall and Cox. 8¾" × 5½", pp. 142. Price: 12s. 6d.

Intended primarily for the "mental hospital doctor".

"Clinical Uses of Intravenous Procaine", by David J. Graubard, M.D., and Milton C. Peterson, M.D.; British Commonwealth Edition, edited by William W. Mushin, F.F.A., R.C.S., D.A.; 1951. Oxford: Blackwell Scientific Publications. 8¾" × 5½", pp. 96. Price: 8s. 6d.

The authors deal with the intravenous use of procaine in many clinical conditions.

"Le tétanos expérimental par la toxine tétanique", by Mario Pelloja; 1951. Paris: Masson et Cie. 10" × 6¼", pp. 300, with illustrations. Price: 1000 fr.

The author deals with the pathogenesis of experimental tetanus and in the light of his own researches discusses the transmission of the tetanus toxin. He holds that the toxin is conveyed to the nervous centres by the circulation.

"Diététique clinique de l'adulte", by Dr. Michel Demole; 1951. Paris: Masson et Cie. 10" × 6¼", pp. 372. Price: 2000 fr.

The author deals with normal nutrition, with general dietetics and with the application of dietetics to various clinical conditions.

"Les stimulines hypophysaires", by André Lemaire, Florian Delbarre and J. P. Michard; 1951. Paris: Masson et Cie. 10" × 6¼", pp. 172. Price: 750 fr.

The authors discuss the hypophyseal hormones from every point of view including their clinical application.

"The Pharmacology and Therapeutics of the Materia Medica (Bruce and Dilling's 'Materia Medica and Therapeutics')", by Walter J. Dilling, M.B., Ch.B. (Aberd.), M.P.S. (Hon.); Nineteenth Edition; 1951. London, Toronto, Melbourne, Sydney and Wellington: Cassell and Company, Limited. 7¼" × 5", pp. 630. Price: 21s.

The book, which has been revised to conform with the British Pharmacopœia 1948, is intended for students and practitioners.

The Medical Journal of Australia

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All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

ENTER BIOPHYSICS.

AT the beginning of this century there was but one chair of biochemistry in Britain and the subject was looked on with some suspicion by professors of chemistry, who maintained that every branch of chemistry should be under their direction. Departments of physiology had conducted teaching in chemical physiology or physiological chemistry, and often when an expert was appointed to take charge of biochemical teaching and research he was placed in a subordinate position to the physiologist. But the science gradually won its way. A Biochemical Society was founded in London on March 4, 1911, and some twenty of the original members are still alive; at present the Biochemical Society is a flourishing body with over 1500 members, and the editors of *The Biochemical Journal* have a hard task in selecting and sometimes condensing the many articles which pour into their office. The first International Congress of Biochemistry was held in Cambridge in August, 1949, and was such a success that a congress committee was set up to arrange future meetings. Now every argument in favour of biochemistry separating off as a fledgling from physiology can be used in support of a similar development in biophysics, as the subject is undergoing rapid expansion and is drawing upon the most recondite principles and the most delicate experimental methods of modern physics. Air travel alone has necessitated much detailed research on the application of physics to the human body. The international journal *Biochimica et Biophysica Acta*, published in New York, is now in its fifth year, but a separate organ for biophysics is really necessary. An earnest plea for adequate recognition of this subject has been published in the American journal *Science* (February 16, 1951) by Ralph W. Stacy, of the Ohio State University, Columbus, entitled "The Status and Development of Biophysics", in which the wide scope of the science is discussed and the benefits to be gained by separate organizations are outlined. There have been, of course, great biophysicists in the past, such as Thomas Young, Hermann Helmholtz and Samuel Haughton, but they were isolated phenomena. As Professor Stacy puts it: "There is little doubt that in the future the field of biophysics will grow to such proportions that the creation of a separate department will be imperative and in some institutions may even now be desirable"; and again: "the only solution to this problem is the establishment of a separate discipline for the pursuit of biophysics". Further: "Even when graduate training of biophysicists is undertaken in physiology departments the degree given should be in biophysics so that the world will know the nature of the training of the individual."

Many of the difficulties and pitfalls which once beset the emergence and pursuit of biochemistry would be present if biophysics were elevated to detached recognition. There are organic chemists with little biological approach who hold biochemical positions, and there are physiologists whose training in chemical principles and methods leaves much to be desired and yet who wish to be regarded as biochemists. Both, however, can do useful work. A similar grouping can be found in biophysics. It is interesting to note that Professor A. V. Hill, whose researches on the thermodynamics of contractile tissue have aroused world-wide recognition, is of the opinion that a trained physicist with but little knowledge of physiology will do better work than a trained physiologist with but little knowledge of physics. This may be true in general, but the physicist should not forget that many of the devices he employs have emanated from physiological laboratories, such as the D'Arsonval and string galvanometers, certain colorimeters and spectrophotometers, and the notation for registering hydrogen ion concentration. There is a veritable danger, it must be admitted, that young enthusiasts may apply highly complicated and costly techniques borrowed from physical engineering to the working of a human organ. Already procedures have been published dealing with the action of the heart which would require elaborate apparatus and a special training to use. Whether these have added to our knowledge or can be recommended in routine study is debatable. To such research workers the Americans apply the term "gadgeteers", and this pungent criticism is often only too just. One serious warning can be given, namely, that, at least for the present, the biophysicist should keep away from pathology.

Another question arises concerning the physical instruments used in medical practice. A doctor, pathologist or histologist can use a microscope to good purpose and yet be ignorant of the complicated mathematical optics upon which the construction is based. A cynical maker of apparatus remarked that an instrument should be foolproof, nurse-proof and doctor-proof. Lastly, there is the unavoidable question how much biophysics the medical student should acquire in his curriculum, which we all know is already overcrowded. Professor Stacy puts the matter thus: "The basic ethics of medicine demand that a physician in treating a patient shall know when he needs a consultation and whom to consult. . . . Physicians need not be biophysicists but they do need an introduction to biophysics sufficiently extensive to tell what is possible and to know where they need to go to learn what they do not know." That biophysics will soon be elevated to a status equal to that of biochemistry we must be prepared to envisage; already the signs of such a development are manifest.

Current Comment.

DRUG ADDICTION.

THE unhappy problem of drug addiction will never be solved without the full voluntary cooperation of an informed medical profession. For this reason attention is drawn to an article on the subject by P. O. Wolff,[1] who is chief of the Addiction-producing Drugs Section of the World Health Organization at Geneva. This article goes far to clarify the confusion between addiction and habit and to establish a definition of addiction; it contains information on methods of recognizing addiction-producing properties in a drug; and it concludes with pertinent comments on some of the newer drugs. Wolff points out that to define drug addiction correctly it is first necessary to make a fundamental distinction between habit and true addiction. Habit, of course, has a wider connotation than its pharmacological use, and it is important to have a definition that applies primarily to the substances concerned in the present study. After long deliberation the Expert Committee on Drugs Liable to Produce Addiction, of the World Health Organization, has arrived at the following definition of "habit-forming", in the relevant sense:

> A habit-forming drug is one which is, or may be, taken repeatedly without the production of all the characteristics outlined in the definition of addiction and which is not generally considered to be detrimental to the individual and to society.

This definition will be clearer if reference is made to the definition of drug addiction prepared by the same committee:

> Drug addiction is a state of periodic or chronic intoxication, detrimental to the individual and to society, produced by the repeated consumption of a drug (natural or synthetic). Its characteristics include:
>
> (1) An overpowering desire or need (compulsion) to continue taking the drug and to obtain it by any means;
>
> (2) a tendency to increase the dose;
>
> (3) a psychic (psychological) and sometimes a physical dependence on the effects of the drug.

The definition of a habit-forming drug thus covers the non-addiction-producing drugs in the full sense, such as tobacco, coffee and others. The definition of addiction, Wolff states, "applies to all the substances embodied in the various diplomatic instruments and has, for this reason, been drawn up very carefully in order to avoid mentioning a symptom which would not be observed in all the types of addiction". Both definitions have been adopted by the Executive Board of the World Health Organization. From the general point of view, Wolff states, drug addiction is characterized by euphoria (at a certain stage), by tolerance of the dose absorbed (without, however, the extension of this tolerance to all centres and all effects), and by physical and psychic dependence. The physical dependence is characterized by a change in certain normal functions which necessitates continuous administration of the drug. But psychic dependence may be considered the essential feature of drug addiction. The decisive factor which proves the addiction and determines the diagnosis is a psychosomatic syndrome typical of abstinence, comprising psychic and physical phenomena, the latter being due to "deformed" physiological processes. During drug addiction the cellular functions of the individual demand the presence of the drug. The drugs able to produce true addiction have the property of creating addiction in all persons who take them long enough in sufficiently large doses. If psychic fixation phenomena do not occur, or are of lesser degree, physical subjugation is nevertheless established; but when the psychic constituent of addiction is non-existent, or nearly so, it is proper, according to Wolff, to speak of a chronic malady due to the drug and not of an addiction proper. Thus the inherent tendency of the substance to produce addiction is one of the principal characteristics of the drug. However, the period necessary for development of addiction and the degree to which it may attain depend on the personality of the subject. The essential property of producing addiction distinguishes the substances concerned from the group used by "habit", for example, tobacco. Many smokers, even heavy smokers, can stop smoking at any time, for "the active substances of tobacco do not enter into their cellular metabolism"—or at least this has never been demonstrated. Difficulty in breaking the tobacco habit, or the manifestation of neuropathic symptoms, is due to the smoker's individuality and not to the substance. A certain tolerance is developed to tobacco, but this does not correspond to the classical form of true tolerance which automatically necessitates the increase of the dose in order to avoid abstinence symptoms. Wolff asserts that there is no certain proof that true addiction can be voluntarily abandoned as can the tobacco habit; the possible cases of withdrawal without medical aid may, he suggests, be counted among the very rare exceptions which always present themselves in the biological field.

Tolerance is an important aspect of drug addiction; it is stated to signify "only that the reaction of the organism to the same dose of substance, repeatedly administered, has diminished little by little, and that a functional adaptation has taken place so that, to reproduce a similar or equivalent effect, larger and larger doses of the same substance must be administered". Tolerance may be the first indication that a substance can produce addiction. Different types of tolerance exist: pharmacological tolerance in respect of certain medicaments which do not produce addiction, for example, organic nitrites; individual tolerance, for example, that of many persons for caffeine; the tolerance of certain animal species in respect of some drugs, for example, that of rabbits for belladonna. Another important effect is known as "crossed tolerance": a subject with tolerance for an addiction-producing substance equally tolerates another substance having analogous properties. Crossed tolerance gives a valuable indication of the liability of the second substance to produce addiction. The importance of this is shown as Wolff goes on to discuss the recognition of addiction-producing drugs. It is important, of course, that this be done before a drug is allowed into general use, but it presents practical difficulties. Observations made on animals have only a limited value. Of the three principal manifestations of addiction, tolerance and, to a much more limited extent, physical dependence may be investigated with animals; the third manifestation, psychic dependence, is to be observed only in man. A clear indication of the addiction-producing qualities of a drug can be obtained only from prolonged experience of its use in man; but information of value can be obtained more rapidly by examination of the substance in comparison with other known substances for the production of euphoria in former addicts and for the possibility of substituting it for morphine in morphine addicts. Use is therefore made of the phenomenon of crossed tolerance. The view of the Expert Committee on Drugs Liable to Produce Addiction is that all available evidence indicates that any substance which will sustain an established addiction (that is, will adequately replace the drug which has produced the addiction) must be considered as also capable of producing addiction. Wolff describes the method of investigation known as the Lexington test, which is based on these principles and answers criticisms that have been made of the test. According to the facts at present known, he states, the test gives trustworthy results.

Many substances have been brought forward in the belief that they had morphine-like effects but did not produce addiction, and then the claims were proved unjustified. It is startling to realize that diacetylmorphine (heroin) was launched some fifty years ago in these circumstances; a modern example is pethidine. The arrival on the market of such drugs, with their unrestricted sale because of their "harmlessness", has had two serious consequences: primary addiction has been created from the unwary taking of the drug in good faith, and addicts who would otherwise have submitted to treatment have

[1] *The Journal of Pharmacy and Pharmacology*, January, 1951.

had a means to satisfy and so perpetuate their addiction. Wolff refers to instances of what he charitably calls carelessness, in which drugs have been launched without due precautions and persisted with as harmless, despite contrary evidence. The harmlessness of both methadone and ketobemidone has been maintained in certain European countries despite the clear demonstration of their addiction-producing qualities in Anglo-Saxon countries. It should be widely known of methadone in particular that clear cases of addiction have occurred, in some instances almost certainly as a direct result of the insistence on its harmlessness; Wolff quotes two doctors and a whole family among those addicted to methadone. There is evidence to suggest that some medical practitioners in Australia have similar mistaken ideas of the drug's harmlessness and have, in all innocence, prescribed it rather freely—for example, in orally administered forms for minor pain. It now comes under the "dangerous drugs" provisions in most, if not all, States of the Commonwealth, but for effective control full appreciation of a drug's qualities by the prescriber is more important than legislative measures, necessary as these are.

Diacetylmorphine (heroin) still remains a problem to those concerned with addiction on a world scale. Its manufacture and sale are now forbidden in 24 countries, but others, including Australia, still regard it as indispensable. Wolff pleads that the question of the manufacture and sale of diacetylmorphine, "the most dangerous of the morphine derivatives generally available", should be considered as an international matter. The international struggle against its abuse, he asserts, will not be brought to a satisfactory conclusion as long as there is still "legal" diacetylmorphine in the world. Cooperation in this in the interest of all would be a good example of international cooperation, even when the drug seems to offer no local problem.

Wolff has a good deal more to tell of modern drugs of the addiction-producing group. His article will repay reading in full. Two of the main impressions it leaves are that drug addiction is an international problem made more difficult by local unwillingness to cooperate and that the World Health Organization's handling of the problem is in line with the intelligent work done under the ill-fated League of Nations.

SYNERGISM AND ANTAGONISM OF ANTIBIOTICS.

THE synergic and antagonistic action of drugs has been known for a considerable time, though some of the old-fashioned prescriptions might suggest that the composer was either very well versed in this aspect of pharmacology or else very trusting. In modern practice the prescriber more often administers single preparations or combinations found to be more effective than the single components. As the old galenicals gradually fade away so the newer knowledge of the pharmacologist, based on the relationship of molecular structure, or on the experience of controlled experiment, or both, has greatly encouraged the study and application of the properties of antagonistic and synergic action in prescribing. It is natural that this branch of knowledge lags somewhat behind the clinical introduction of new therapeutic substances, but when gained it may enhance the potency of drugs, and at the same time ensure greater safety in their use. A good example of this is in the action of a combination of sulphonamides, which may now be regarded as standard practice. Antibiotics suggest themselves as a possible field for useful research, and examples of synergism between antibiotics or between an antibiotic and a completely different substance will come to mind. Multiple therapy with these substances is now in greater demand, especially since supplies have been increased and, in some instances at least, costs have been reduced. That more accurate knowledge is required on this subject will be agreed, and E. Jawetz, J. B. Gunnison, R. S. Speck and V. R. Coleman have supplied some useful information concerning antagonism which has been found with chloramphenicol and penicillin.[1] They remark that synergistic action has been observed between penicillin and streptomycin in certain infections and that brucellosis, always a resistant disease, yields better to a combination of antibiotics than to any single substance. But reports that penicillin may be hampered in its action by some other preparations of similar type led them to carry out tests on chloramphenicol and penicillin *in vitro* and on mice infected by the test organisms. The organisms used were virulent strains of a β hæmolytic streptococcus and a *Klebsiella pneumoniæ*. The number of organisms which proved lethal to mice after intraperitoneal injection was known, and was maintained at a constant level by frequent passage through mice. Commercial sodium penicillin G and synthetic chloramphenicol ("Chloromycetin") were used, and the media employed were standard products. Scrutiny of the results of the in-vitro tests showed that chance might vary the counts of viable bacteria so as to show twofold or threefold differences, hence only differences of tenfold or greater were regarded as significant. Mice of a heterozygous stock were used in groups; the antibiotics were administered within one to four hours after the inoculation, and equivalent groups of untreated controls were observed. Differences in death rates were counted as significant only when they exceeded 30%. It was found that the "Chloromycetin" interfered with the action of penicillin, preventing its early bactericidal effect, and this interference was demonstrable over a wide range of concentrations and proportions of the drugs. *In vitro* the cultures were eventually sterilized by the penicillin, but *in vivo* the death rates of the animals were greater in spite of penicillin when the "Chloromycetin" was given within a few minutes of the other injection. However, "Chloromycetin" did not suffer any interference in its action by the giving of penicillin shortly afterwards. Thus the antagonism was not a mutual phenomenon. It seems curious that relatively inactive concentrations of "Chloromycetin" could antagonize penicillin even in effective concentrations. With active concentrations of "Chloromycetin" or those without bactericidal effect no interference occurred. Similarly, large or ineffective amounts of penicillin masked any such action. The authors considered that on the basis of their experimental results either of two hypotheses might account for this phenomenon. The possibility of physical or chemical action they reject as contrary to the evidence, and think rather that one drug acts on the organisms and so modifies them as to reduce their sensitivity to the other drug. Such modification might be on growth, multiplication, division or enzyme activities. That there is some relationship to the biological activity of the microorganisms seems highly probable, since "Chloromycetin" does not interfere with penicillin if the latter acts first. As the early bactericidal action of penicillin wanes so the antagonism of "Chloromycetin" also diminishes. This finding agrees with experiences with the synergic effect of streptomycin with penicillin, for the organisms unaffected by the early action of penicillin are those which are successfully attacked by streptomycin. Further details of these experiments on antagonism need not be given here, but it is clear that there are clinical implications. It is also interesting to note that a synergistic drug like streptomycin can overcome the antagonism of "Chloromycetin". Since true mutual antagonism does not exist, it is all the more important that the exact mechanism of the action of antibiotics should be closely studied, in particular the characteristics which affect the susceptibility of microorganisms. This has of course been in the forefront of research since the astonishing properties of penicillin were discovered, and promises to add more to the fundamentals of knowledge of bacterial infection. Whatever may be the shortcomings of the present age, no modern Zechariah could accuse it of despising the day of small things.

[1] *Archives of Internal Medicine*, March, 1951.

Abstracts from Medical Literature.

PHYSIOLOGY.

Thermal Gradients in the Vascular System.

S. M. HORVATH, A. RUBEN AND E. L. FOLTZ (*The American Journal of Physiology*, May, 1950) state that most observations of body temperature have been limited to measurements of the temperature of the various easily accessible body cavities or to skin and subcutaneous and muscle tissue. In a series of experiments with dogs thermocouples were inserted in many places throughout the circulatory system and compared with the readings in the more usual situations. The authors report that the temperature of the blood throughout the vascular system is not constant. Its absolute value at any point is dependent upon both the relative metabolic level of the tissues through which it passes and the temperature of the blood with which it mixes. Pronounced thermal gradients were observed not only in the peripheral blood, but also in the blood draining the organs of the body core. Observations on the temperature of blood in such sites as the coronary sinus, renal vein and other areas are reported, and their general relationships to the temperature of other areas and their importance to physiological function are discussed.

Rate of Cooling in Immersion Hypothermia.

R. C. WOLFF AND K. E. PENROD (*The American Journal of Physiology*, December, 1950) report a statistical study of the factors which affect the rate of cooling of anæsthetized dogs immersed to the neck in an ice bath. The factors investigated include surgical manipulations, hair covering, shivering intensity, body size and sex. Even relatively slight surgical manœuvres were found to decrease significantly the rate of cooling. It is suggested that the adrenal gland may contribute to this response. A heavy coat of hair offered significant protection against cooling, but short hair proved no better than no hair. Shivering was found to have a significant effect in slowing the cooling rate, but a minimal shivering showed a tendency toward an increased cooling rate when comparing with no shivering. Although a definite trend toward slower cooling with increasing body size exists, the differences were not found to be statistically significant. No difference between sexes was detected in the cooling rate.

Changes in Thoracic Duct Lymph after Total Body Irradiation.

C. S. BROWN, E. HARDENBERGH AND J. L. TULLIS (*The American Journal of Physiology*, December, 1950) report that studies were conducted on thoracic duct lymph and blood in normal dogs and in dogs exposed to 500r total body X-radiation. Lymph total protein content fluctuated within the first fifty hours after irradiation and then decreased at a slow, even rate. Uric acid and non-protein nitrogen levels in lymph increased within four hours after irradiation, but later decreased to slightly below normal. Lymph creatinine levels decreased within four hours after irradiation. After eighteen hours the level rose gradually toward the normal. Sugar and chloride levels showed no appreciable change. The total number of white blood cells in lymph dropped precipitously within four hours after irradiation, and remained at a low level throughout the period of observation. The results of bacterial culture of blood and lymph were negative.

Heart Size in the Intact Animal.

W. F. HAMILTON, J. W. REMINGTON AND W. F. HAMILTON, JUNIOR (*The American Journal of Physiology*, November, 1950), state that the heart size in intact animals is directly correlated with time of diastole, mean systolic pressure, stroke volume and work per beat. Physiological and technical variables produce a wide scatter. Epinephrine infusion produces a slowly beating large heart with high mean systolic pressure, but with diminished stroke volume and work per beat as compared to undrugged dogs. Vagotomy, with epinephrine infusion or with carotid sinus removal, gives a rapidly beating small heart with high mean systolic pressures and diminished stroke volume and work per beat as compared to untreated dogs. These differences persist with bleeding. At high normal venous pressures, reflex changes in diastolic time are paralleled by changes in venous pressure and in heart size. At very low venous pressures the heart may be large or small, depending on filling time. At rapid rates, the heart is small and the venous pressure may be high or low depending on venous return. The most important factor in fixing the diastolic size of the heart, in the intact animal, is the filling time (heart rate).

Massive Transfusion and Hæmorrhage.

A. C. GUYTON, J. E. LINDLEY, R. N. TOUCHSTONE, S. M. SMITH AND H. M. BATSON (*The American Journal of Physiology*, December, 1950) report that transfusion and hæmorrhage at rates less than 0·1 control blood volume per minute have been studied in 74 dogs. At these slow rates the blood pressure appeared to be a function mainly of blood quantity in the animal at any given time and relatively little affected by the rate *per se* of transfusion or hæmorrhage. Increasing the quantity of blood in a dog to as much as 2·62 times the control value caused very little increase in blood pressure, the maximum increase in pressure being an average of 17 millimetres of mercury when the average quantity of blood in the animals reached 1·8 times the control value. At greater quantities than this the pressure fell. Denervation of the pressoreceptors, presumably followed by excess sympathetic activity, resulted in a blood pressure plateau averaging 54 millimetres of mercury above normal when these animals were given slow but massive transfusions. Complete spinal anæsthesia, presumably followed by dormant sympathetics, resulted in a blood pressure plateau averaging 70 millimetres of mercury below normal when the animals were given slow but massive transfusions. Hæmorrhage failed to cause either pronounced or rapid shifts of fluid between the interstitial spaces and the blood-stream. From determinations of hæmatocrits, hæmoglobin values and red cell counts, it appeared that during massive transfusion occurring over an average period of approximately forty minutes, an average of 63% of the transfused whole blood and 113% of the plasma portion of the transfused blood was lost from the circulation by the time transfusion was complete. Relationship of the above findings to the basic physiology of blood volume and blood pressure control in the normal animal is discussed.

Distribution of Blood in the Rabbit's Kidney.

W. INSULL, JUNIOR, I. G. TILLOTSON AND J. M. HAYMAN, JUNIOR (*The American Journal of Physiology*, December, 1950), report that attempts were made to confirm Trueta's hypothesis that renal blood flow may be diverted from cortical to medullary channels under certain conditions. When excised rabbit kidneys were perfused with Prussian blue in 6% acacia solution at low pressures, only the deep juxtamedullary glomeruli were filled, while with higher pressures all glomeruli were filled. Renal blood flow and systemic blood pressure were measured in anæsthetized eviscerated rabbits, and the distribution of glomeruli receiving blood under various conditions was shown by staining with Janus green B after intraarterial injection. The deeper glomeruli were never free from dye when the peripheral ones were stained. In some experiments, after sciatic stimulation, stimulation of the perirenal plexus or hæmorrhage, the juxtamedullary glomeruli were uniformly stained, while those in the peripheral areas of the cortex were unstained. This distribution, which resembled that described by Trueta, occurred only when renal blood flow was low. These experiments furnish no support for the hypothesis that any significant quantity of blood is diverted from cortical to medullary pathways by direct or reflex stimulation of renal vasoconstrictor nerves.

BIOCHEMISTRY.

Choline Esterase.

D. K. MAYERS (*Archives of Biochemistry*, July, 1950) has shown that the affinity of the choline esterases for eserine, "Prostigmin" and certain "Prostigmin" analogues is decreased by increasing the concentration of electrolytes in the medium.

Ammonia Utilization.

H. A. LARDY AND G. FELDOTT (*The Journal of Biological Chemistry*, September, 1950) have demonstrated that young rats fed a diet containing the ten essential amino acids effect a net utilization of supplementary ammonium nitrogen as indicated by improved weight gain and net retention of ammonium nitrogen. Supplements of ammonium citrate do not improve weight gains by rats fed suboptimal amounts of natural proteins. The authors state that this means that with the established exceptions of

lysine and threonine and the possible exceptions of valine and arginine, each of the "essential" amino acids can be replaced in the diet of growing rats by its corresponding α-keto analogue. Thus it is the peculiar carbon skeleton of each of these molecules which is the dietary essential.

H. D. HOBERMAN AND J. GRAFF (*The Journal of Biological Chemistry*, September, 1950) have shown that the amount of isotopic nitrogen excreted by fasting animals receiving isotopic ammonium citrate is more than 50% greater than that excreted by glucose-fed rats.

Amino Nitrogen.

R. C. THOMPSON AND M. ABDULNABI (*The Journal of Biological Chemistry*, August, 1950) report that analyses on twenty-four-hour urine samples from 24 human subjects, 13 male and 11 female, indicate a significant sex difference in the excretion of α-amino nitrogen when expressed as milligrammes per day per kilogram of body weight. This difference is noted in both "free" and "bound" α-amino nitrogen. The amounts of α-amino nitrogen excreted by the male subjects showed a significant correlation with body weight. Such correlation was not observed with female subjects. The authors also give data on urinary excretion of "total" lysine by nine males and seven females.

Alcoholism.

E. BEERSTECHER *et alii* (*Archives of Biochemistry*, November, 1950) have reported data from the investigation of approximately sixty metabolic items over a period of a month in a group of four alcoholics and eight non-alcoholic controls. Six of the items studied show statistically significant differences (at the customary 5% level) between alcoholics and non-alcoholics. Only three statistically significant items would be expected by chance. Thus, the data strongly indicate that compulsive drinkers possess certain common metabolic features. Of the items studied, those that appear to be associated with alcoholism are as follows: elevated levels of sodium and uric acid in saliva; elevated levels of urinary hippuric acid, uric acid, citric acid, unidentified weak acids, pH and pigment; an increased level of magnesium in the blood serum; decreased urinary levels of gonadotropin, turine and citrulline; a decreased phosphorus level in the blood serum; an increased taste sensitivity to sodium chloride.

Androgens.

C. KOCHAKIAN AND E. ROBERTSON (*Archives of Biochemistry*, November, 1950) report that androgens produced a small increase in weight and an increase in proportion to dose in original activity of the kidney of the castrated rat. The alkaline phosphatase was slightly increased in amount and the amount of acid phosphatase changed in proportion to the weight. The arginase activity of the liver was not affected by the androgens, but the alkaline phosphatase showed an irregular but persistent small increase in amount. Hypophysectomy of adult male rats resulted in a pronounced decrease in arginase activity, a slight decrease in acid phosphatase activity, and an increase in alkaline phosphatase activity of the liver. All of these enzymes of the kidney rapidly decreased. Testosterone did not affect the liver enzymes, but it restored the arginase and alkaline phosphatase activities of the kidney.

Tryptophane.

M. HEIMBERG *et alii* (*Archives of Biochemistry*, August, 1950) report that under experimental conditions, the urinary excretion of N-methyl-nicotinamide and quinolinic acid by rats, after being fed 100 milligrammes of *dl*-tryptophane, is inversely proportional to the level of casein in the diet, independent of supplementation by either nicotinic acid or pyridoxine. The increased urinary excretions of xanthurenic acid by pyridoxine-deficient rats after tryptophane feeding is diminished by the addition of nicotinic acid to the diet. Pyridoxine does not appear to be directly involved in the conversion of tryptophane to N-methyl-nicotinamide by the rat.

Serum Albumin.

T. PETERS AND C. ANFINSON (*The Journal of Biological Chemistry*, October, 1950) have developed an immunological technique by which small amounts of serum albumin in chicken liver slices and their incubation media may be determined. The standard albumin was obtained by isolation from chicken serum. It was shown that chicken liver slices, upon incubation in bicarbonate medium, produce a net quantity of serum albumin of about 0·12 milligramme per gramme of liver per hour. In a chicken weighing 2·5 kilograms, it was calculated that the liver could replace the total circulating albumin in fourteen days. No consistent effects were observed upon the addition of amino acid mixtures or oxidizable substrates to the media during incubations. No significant change in the rate of albumin production was found upon addition to the incubation medium of insulin, thyronine, growth hormone, adrenal extract, cortisone or desoxycorticosterone.

Brain Phosphatase.

F. BINKLEY AND C. ALSON (*The Journal of Biological Chemistry*, October, 1950) have obtained a brain phosphatase in a purified condition. It was found to hydrolyse inorganic pyrophosphate and to remove the terminal phosphate of ATP. The activity of the enzyme was found to depend upon the presence of magnesium ions. Considerable activation was observed when glutathione was added together with the magnesium, but maximal activity was obtained only by preincubation of the enzyme with magnesium and glutathione.

Adrenaline.

M. SOMOGYI (*The Journal of Biological Chemistry*, October, 1950) has reported experiments showing that adrenaline strongly depresses the rate of peripheral glucose assimilation. According to the author, available observations on intact animals furnish no basis for the currently accepted concepts that the hyperglycæmic response to adrenaline action is an obvious result of accelerated hepatic glycogenolysis. While such a response may (and even is likely to) take place, depression of the rate of glucose assimilation both in the liver and in the peripheral tissues, which is caused by adrenaline, can readily account for a rise of the glycæmic level, without requiring any acceleration of the hepatic glycogenolysis.

Anæmia.

I. C. WELLS AND H. A. ITANS (*The Journal of Biological Chemistry*, January, 1951) have determined the ratio of the amount of sickle-cell anæmia hæmoglobin to that of normal hæmoglobin in 42 sicklæmic subjects who were otherwise normal and genetically unrelated. In this series the sickle-cell anæmia hæmoglobin value varied from about 24% to 45%. Of the several factors tested, that is, time, age, sex, some environmental factors, and heredity, the last is the only one not excluded as having an appreciable influence on the ratio of the two amounts of the hæmoglobin which occurs in a sicklæmic person. The discovery of some anomalous cases of sickle-cell anæmia is reported. In these cases the subjects, in contrast to the true sickle-cell anæmic, are able to produce small amounts of normal hæmoglobin.

Ferritin.

A. MAZUR *et alii* (*The Journal of Biological Chemistry*, December, 1950) have shown that the normal aerobic liver contains ferritin almost entirely in the inactive disulphide state. Anaerobic incubation of the liver produces a progressive increase in the amount of active sulphydryl ferritin, together with an increase in the amount of reduced glutathione. Liver slices in oxygen oxidize active sulphydryl ferritin to the inactive disulphide state. The extent of this reaction is a function of the oxygen tension. The inactivated disulphide ferritin can be reactivated with cystine or reduced glutathione. Conversely, liver slices in the absence of oxygen convert disulphide ferritin to the active sulphydryl form. A cell-free solution, in which liver slices had been incubated aerobically, is also capable of inactivating the vasodepressor activity of ferritin under aerobic conditions. This inactivation is also accompanied by oxidation of the sulphydryl ferritin to the disulphide form. It is postulated that the system within the liver cell which is concerned with the vasodepressor function of ferritin is dependent on equilibrium between disulphide and sulphydryl forms of ferritin. This equilibrium is affected by oxygen tension, as well as by other biological stimuli *in vivo*. A role for glutathione in this system is suggested.

Insulin.

A. N. WICH *et alii* (*The Journal of Biological Chemistry*, January, 1951), using radioactive glucose, have shown that insulin acts on the extrahepatic tissues to increase greatly their combustion of glucose to carbon dioxide. Eviscerated rabbits were used. The action is not immediate, there being a lag in the appearance of radioactive carbon in the expired carbon dioxide in comparison with the control animals. During this time large amounts of glucose disappear from the blood and enter metabolic pools. The extra glucose which disappears under insulin action and is not oxidized is disposed of chiefly as water-soluble compounds with lesser amounts in glycogen and protein-like material.

British Medical Association News.

ANNUAL MEETING.

THE annual general meeting of the Western Australian Branch of the British Medical Association was held in the nurses' lecture room, Princess Margaret Hospital for Children, on March 21, 1951, DR. K. G. ABERDEEN, the Vice-President, in the chair. Thirty-five members of the association were present.

MINUTES.

The minutes of the annual general meeting held in March, 1950, were confirmed.

HONORARY TREASURER'S REPORT.

The honorary treasurer's report for the year 1950 was confirmed.

PROTECTION OF PRACTICES.

DR. F. W. CARTER gave a résumé of the work of the Protection of Practices Committee from its inception up to the present time. He explained that the scheme had been started for the purpose of protecting the interests of members of the Branch absent from their practices on war service, and for the rendering of financial assistance to certain other members of the association whose war service had interrupted post-graduate studies or who were desirous of commencing in practice, but whose resources were limited. It sought first to protect the practices of absentees. Experience gained during the course of the Great War of 1914-1918 had shown the necessity for that. It envisaged secondly a future need of financial assistance to the dependants of absentee members—if that absence extended into years—continuing after the absentee's return so incapacitated as to render such assistance necessary, and thirdly, assistance in the rehabilitation of ex-service members (mainly young men) by grants to enable them to live decently during post-graduate studies and by loans at a "peppercorn" rate of interest for the purpose of setting up practice after the war.

Dr. Carter said that the protection of practices was obviously an ethical matter; it was under the control of a committee of the Branch Council. Much of its work was behind the scenes, but despite that—or even because of it—the results achieved had been, as one would have expected, very good. In a few cases only had any difficulty been experienced in persuading a newcomer not to enter protected territory. A practitioner did not need to be shown the justice underlying such action, whether he was a member of the scheme or not. Under the heading of "protection" was the clause that provided that one-third of the fees received by a doctor for treatment of the patients of absentees should be remitted to the scheme for transmission to an agent of the absentee. A large sum had passed through the fund in that way, but large amounts did not, when by special arrangements between resident doctor and absentee, moneys were paid direct to the legal representative of the absentee. Notwithstanding the difficulties associated with that department of the scheme's activities—and it should be remembered that not all of the members of the Branch were contributing members of the scheme—thousands of pounds had been transferred to absentees for work done by others during their absence. When one remembered what had taken place during the Great War of 1914-1918, it could be said that professional standards were never so high as during the war so recently past.

Dr. Carter went on to say that preparations to form the scheme had begun soon after the onset of war, in September, 1939. A number of meetings were held and it was finally decided, in March, 1940, that such a scheme be put into operation immediately. Terms and conditions were embodied in a trust deed. Control was vested in three trustees, Dr. F. W. Carter, Dr. L. A. Hayward and Dr. M. Kasner Moss. On the death of Dr. Moss his place was filled by Dr. H. H. Stewart. They were the trustees at the present time. The method of collecting contributions to the fund was by the striking of a rate based on the net profit as shown by members' income tax returns, at a commencing rate of 3·80 pence in the pound on an income of £600, and increasing as the income increased by 0·005 pence in the pound. That contribution to the fund was known as the levy and was not payable by any member whose taxable income was less than £600 after there had been allowed as deductions from the figure shown as taxable income for the Taxation Department, all income taxes paid, life insurance up to £100, and an allowance for the member's wife and family. Those deductions limited the number of contributors considerably, but many members who were not liable for the levy had made donations to the fund. Those donations amounted to over £800. As income tax increased during the war, and as it was a deduction for purposes of calculating the levy, so the levy became progressively smaller. By April 24, 1940, the number of members who had joined the scheme was 137, and the membership had ultimately reached 160. Although there had been 181 names on the register, deaths and a few resignations prevented that number from being attained at any one time. The present number of members was 148.

Dr. Carter said that altogether over the eleven years for which the scheme had been in operation, the amount received from the levy and donations had totalled £12,457 18s. 6d. During the early days of the scheme, the demands on it had been relatively few, and moneys in hand had been invested from time to time in Commonwealth Government loans. Interest earned on those and on loans to members totalled £1627 17s. 1d. That was subject to Federal income tax, and altogether £377 8s. 6d. had been paid in tax. Since the inception of the scheme £12,905 19s. had been advanced to members in the form of loans to be repaid, or as grants, in cases in which repayment would impose a burden. The rate of interest charged was 1% *per annum*. The trustees had sought for reasons why such a loan should be granted rather than for reasons why it should not. Thus securities played but a small part in the transactions of the scheme. Under general headings the following loans and grants had been made:

	£	s.	d.
For maintenance of life insurance policies and payments of instalments on houses and on other assets during the absence of a beneficiary at war	1261	11	0
For payment of pressing liabilities of members	234	11	1
For payment of expenses whilst a member was on special work, or whilst a practice was being established	1622	0	0
For purchase of practices or shares in practices	5995	9	8
For purchase of instruments, cars, furniture *et cetera*	3951	9	8
For expenses in relation to illness resulting from the war	350	0	0
Total	£13,415	1	5

Dr. Carter said that that total exceeded the actual cash paid out by the amount of a loan taken over by a member from one leaving the State. Loans made had amounted to £11,401 12s. 7d. and grants to £2013 8s. 10d. The amount owing to the fund in February, 1951, on account of loans to members was £7767 18s. 11d. The cost of administration for the ten years to February 28, 1951, had been £1292 18s. 8d., including the salary of secretary and staff, the provision of office premises, printing, stationery, postage and revenue stamps, legal and audit costs, and sundries.

Dr. Carter pointed out that the scheme was not one for the provision of cheap money to buyers of practices. It had helped many young men to acquire practices or partnerships. There were conditions binding on the trustees which must be met if help was to be given, but the trustees had been guided more by the spirit which prompted the inauguration of the scheme than by a meticulous observance of those conditions. It was urged, however, that if the scheme was to continue to operate, beneficiaries would recognize the importance of a discharge of their liabilities towards the fund as soon as they were financially able to do so. Only by observance of that would other members of the profession receive the welcome approval when, in their turn, they applied for some temporary assistance to tide them over the initial difficulties of practice ownership.

In conclusion, Dr. Carter said that the thanks of the trustees were extended to Mr. E. S. Hart for years of faithful service; the scheme had provided practically a whole-time job for the first year or so, and they regarded his charges throughout as being moderate in the extreme while his integrity was undoubted. The utmost secrecy regarding individual transactions had been observed, so that outside the three members comprising the trustee body, no one other than Mr. Hart was cognizant of the fund's transactions.

Dr. H. Stewart paid tribute to the work done on the committee by Dr. Carter and said that he felt that Dr. Carter was mainly responsible for its success.

THE BRANCH LIBRARY.

Before the report of the library committee was read the vice-president expressed the appreciation of the association to the chairman, Dr. H. S. Lucraft, for the great amount of work he had done to bring the library up to its present efficiency.

Dr. Lucraft then read the Library Committee report in which it was stated that the committee had met on ten occasions during the year and a report on library matters was submitted to the Council each month. The committee was very pleased to report that the amount of interest displayed in the library continued to increase and on all sides were heard expressions of appreciation at the very greatly improved facilities it had to offer. The committee felt that there was, or soon would be, in Western Australia a library that would compare more than favourably with any other of its kind in the Commonwealth. Approximately two thousand five hundred requests for information had been received during the year. That figure represented 2100 actual visits to the library and 400 requests received by telephone and letter, and showed an increase of 650 over the figures for the corresponding period of the previous year. Nearly 500 books had been borrowed as well as more than 2700 periodicals, photostats, reprints of articles, extracts *et cetera*.

The library received approximately 130 periodicals. The majority of those were on subscription, some were received *gratis* from the publishers, and the remainder were very generously donated by members. All the more important of the periodicals were being bound. The committee considered that the collection in the library was very representative and, with the addition of a very few new titles, would cover all needs for the immediate future.

As at December 31, 1950, the Cyril Bryan Library Fund stood at £226 6s. 3d. Another account, known as the "Library Donations Account", had been started during the year. It had tided the library over a difficult period and had made it possible to add a number of books of reference, important monographs *et cetera*, which were urgently needed. The fund was administered by the committee with strict and almost parsimonious economy. The unexpended portion of the fund was being held against any future emergency that might arise in connexion with the library's needs. Both funds were still open. The committee was most grateful to all members and others who had contributed to the two funds and had made gifts to the library. The committee also acknowledged with thanks the assistance it had received from the Medical Board, which had made the following grants: 1948, £700; 1949, £300; 1950, £750; 1951, £750. In a recent report to the Council the committee had pointed out that a grant of £750 *per annum* was the absolute minimum on which it could make do. The grant for 1951 was to be allocated in the following way: subscriptions to periodicals, £400; purchase of books, £150; binding of periodicals, £150. The remaining £50 was to be held against rising costs *et cetera*.

The question of the purchase of a microfilm reader was again being considered.

For some time the committee had been considering the need to set aside one section of the library to house all material of an historical nature. With the aid of the W. Horner Nelson Bequest, amounting to some £50, that had become possible, and plans were in hand. Quite a number of articles had already been received and members were urged to make a gift to the library of old books, surgical instruments, medicine chests, photographs *et cetera* for which they had no further use.

The committee had also adopted a bookplate, designed by the architect, Mr. Marshall Clifton, which would be affixed to the inside front cover of all books and bound volumes of periodicals in the library.

The committee considered that a catalogue of the contents of the library should be published. At the present time members were advised, through the "Library Notes", of all new publications as they were received. It would then only be a matter of collecting that information every year or two and issuing it as a supplement to the main catalogue. The question was one of finance; as soon as that was overcome the project could be proceeded with. The committee was particularly happy about the "Library Notes" because it had become increasingly apparent that the inclusion of references to pertinent articles in current periodical literature had proved a very popular and useful innovation amongst members.

The library had borrowed extensively from Branch, college, university and departmental libraries in the eastern States and at home, and on every occasion had received the utmost cooperation and courtesy.

The amount of research work performed in the library had steadily increased during the past year. With the greatly improved book and periodical stock it was possible to supply not only the very latest information on a given subject, but also a consensus of world opinion on it. To keep up to date, contents lists of all the periodicals were made as soon as they were received.

Country members were making greater use of the library, and every effort was made to ensure that they received the required information as soon as possible.

The committee expressed its appreciation of the help of Mr. Hugh Hancock and of the work of the librarians, Miss Bryan and Miss Gee.

The report was received.

INVESTMENTS.

The honorary treasurer, Dr. H. Macmillan, gave a short résumé of discussions in Council on the advisability of investing funds of the association (recently invested in government bonds) in industrial stock carrying a higher rate of interest.

MEDICAL BENEVOLENT FUND.

Dr. J. L. Day read the report of the Medical Benevolent Fund, in which it was noted that income received from subscriptions through the British Medical Association together with a bequest from the estate of the late Dr. W. H. Nelson and interest on treasury bonds and savings bank account had amounted to £535 12s. 5d. Expenditure was in the form of benevolent contributions to two aged or incapacitated doctors and to five doctors' widows and amounted to £334 6s. 8d. A surplus remained for the year of £201 5s. 9d. Invested funds remained the same at £1700; this with a bank balance of £437 4s. 10d. totalled £2137 4s. 10d.

The report was received.

ANNUAL REPORT OF COUNCIL.

The annual report of Council was read by the honorary secretary and received. The report is as follows:

The President and members of the Council of the Western Australian Branch of the British Medical Association have much pleasure in presenting the fifty-second annual report of the work of the Branch for the year ending March 15, 1951.

Membership.

The membership of the Branch has steadily increased during the twelve months under review, and with the total number of members at 462 shows an increase of 24 compared with last year's total of 438, this being due no doubt to the fact that at this stage last year there were a number of resident medical officers who were not members of the association; Council decided to bring the matter before the honorary staff, and the result has been most gratifying. It is interesting to note that the increase in membership during 1950 was only three.

The gains were:		
New members	29	
Transferred from other Branches	34	
	—	63
The losses were:		
Members transferred from this Branch	33	
Resignations	2	
Deaths	4	
	—	39
		—
		24
		—

It is with pleasure that we advise that Dr. S. Mathews completed fifty years as a member of the British Medical Association and has therefore become a life member. We take this opportunity of congratulating Dr. Mathews.

Obituary.

With deep regret we record the deaths of the following members during the year: Dr. W. S. Myles, Dr. H. H. Field-Martell, Dr. L. T. Gillespie and Dr. A. Mayrhofer, also Dr. S. L. Harke and Dr. E. W. Byron. The sincere sympathy of the Branch is extended to the families of these late members.

Meetings.

In addition to the annual meeting, eight general meetings of the Branch were held, including two clinical meetings and one combined medico-legal meeting. At the latter meeting a panel of four lawyers and three doctors discussed medico-legal subjects selected from questions submitted by members of both professions and provided a most interesting evening to the large representative audience.

The subjects of meetings were as follows:

April: "Osteoarthritis of the Hip", Dr. Henry Hill.

May: "Certain Aspects of Allergy", Dr. E. G. Strahan.

June: "Education of the Deaf", Dr. A. W. G. Ewing, M.A.

July: Clinical meeting at the Royal Perth Hospital.

August: "Digitalis in Heart Failure", film evening.

September: Combined medico-legal meeting.

October: "Work in Hospitals in Brompton and Midhurst", Dr. A. H. Penington.

November: Clinical meeting at the Fremantle Hospital.

Council Meetings.

Eighteen meetings of the Council were held. The record of attendance is as follows:

Dr. A. B. Wilson, President	15
Dr. K. G. Aberdeen, Vice-President	17
Dr. B. W. Buttsworth, Chairman of Convocation	15
Dr. F. W. Carter, Federal Council representative	16
Dr. H. Leigh Cook, Federal Council representative	18
Dr. O. R. Corr, Chairman of Contract Practice Committee	12
Dr. D. E. Copping, Councillor (leave of absence eight months)	5
Dr. B. St. P. Gillett, Honorary Secretary	15
Dr. B. A. Hunt, Past President	12
Dr. L. I. Henzell, Commissioner of Public Health	7
Dr. A. F. Janes, Councillor	10
Dr. H. Macmillan, Honorary Treasurer (three months' leave of absence)	13
Dr. A. A. Merritt, Councillor	12
Dr. J. A. McAuliffe, Councillor	8
Dr. Ross Robinson, Councillor	14
Dr. H. M. Trethowan, Assistant Honorary Secretary	14

Office Bearers and Councillors.

The following members have been elected as office bearers for 1951:

President: Dr. K. G. Aberdeen.

Vice-President: Dr. John Day.

Honorary Treasurer: Dr. R. G. Linton.

Honorary Secretary: Dr. J. H. Stubbe.

Honorary Assistant Secretary: Dr. L. P. Gray.

Chairman of Convocation: Dr. B. W. Buttsworth.

The following members have been elected as the five ordinary members of Council for 1951: Dr. P. W. Atkins, Dr. B. O. Bladen, Dr. D. E. Copping, Dr. S. E. Craig, Dr. A. Daly Smith.

Federal Council.

Dr. F. W. Carter and Dr. H. Leigh Cook have again represented the Western Australian Branch on the Federal Council over the past twelve months, and on behalf of all members we would like to express to them our sincere appreciation of their untiring efforts during a very strenuous year. Dr. Carter and Dr. Leigh Cook have been reelected Federal representatives for the ensuing twelve months.

Library.

The report of the library committee will be heard in full, but the Council wishes to thank the chairman of the library committee, Dr. H. S. Lucraft, the committee and the library staff for their cooperation and for increasing facilities of the library, this being made possible by their keen interest and attention to this most important factor of our association. We would also like to thank members who made donations of books, periodicals and certain office fittings, all of which are very much appreciated. We would also like to place on record our appreciation of two sums of £750, making a total of £1500 granted to the Branch by the Medical Board, one grant being made during 1950 and the other for the ensuing year.

Representation.

The Branch was represented by the following members at various meetings and conferences during 1950:

Council of the British Medical Association, London.—Dr. Miles Formby.

Federal Council of the British Medical Association in Australia.—Dr. F. W. Carter, Dr. H. Leigh Cook.

University Advisory Board in Medicine.—Dr. B. A. Hunt.

Australasian Medical Publishing Company, Limited.—Dr. F. W. Carter.

The Editor of "The Medical Journal of Australia".—Dr. H. M. Trethowan.

The State Health Council.—Dr. B. W. Buttsworth, Dr. H. Leigh Cook, Dr. A. B. Webster, Dr. M. F. Williams.

Nurses' Registration Board.—Dr. L. E. Le Souef, Dr. G. A. Thompson.

Dental Board.—Dr. I. O. Thorburn.

College of Dental Science.—Dr. I. O. Thorburn.

Workers' Compensation Act—Underwriters' Joint Committee.—Dr. R. D. McKellar Hall, Dr. K. G. Aberdeen, Dr. N. H. Robinson.

Saint John Ambulance Association.—Dr. A. L. Dawkins.

State Health Council.

Since its inauguration in September, 1949, the State Health Council has met monthly under the chairmanship of the Commissioner of Public Health, Dr. C. E. Cook, and since March, 1950, Dr. L. I. Henzell. The Council has considered a number of health and medical problems during the year and has formulated and submitted medical policy to the Government on such matters as have come to its notice.

Government Medical Officers.

Repatriation Medical Officers' Association.

Our Branch has given all possible help to the Repatriation Medical Officers' Association in the furthering of their claims during the last year for improved conditions of service and salaries, and particularly in regard to the administration of repatriation services.

Salaried Medical Officers.

During the year the matter of remuneration and terms of service of medical consultants to the Repatriation Department came under close scrutiny in view of the stand taken by the department. This matter is still receiving consideration, and the Council will, if necessary, make recommendations to members as to what action they should take with the department, but the Council hopes there will be an early and satisfactory settlement.

Public Health.

We wish to take this opportunity of thanking Dr. L. I. Henzell, Commissioner of Public Health in this State, for his close cooperation and help during the past year, and to assure him of this association's desire that the happy relationship we have so far enjoyed will continue during 1951.

National Health and Medical Services.

During the past year we have seen the first steps towards the objective of a national health scheme. This matter has been discussed in full at recent convocation meetings, and we in this State have agreed to the scheme in principle with certain reservations guarding the independence of the profession in particular from regimentation and government red tape. Our next step is to ensure that the administration of the service does not come within the scope of complete political control.

Pensioner Medical Service and Pharmaceutical Benefits Act.

The pensioner medical service and *Pharmaceutical Benefits Act* have come into operation and according to various reports are working as smoothly as can be expected during

the early stages. The implementation of these schemes, however, has not been fully completed as yet, and the Council is looking forward to the various loose ends being tidied up at an early date.

Australasian Medical Publishing Company, Limited.

The Branch now holds debentures to the value of £1021 approximately, and this money as you know is being held for a building fund to which the British Medical Agency Company has offered its support.

Workers' Compensation Act.

Negotiations were concluded last year between British Medical Association representatives and the Underwriters' Association representatives in connexion with a new schedule of fees for workers' compensation cases. The schedule was printed and came into operation on July 1, 1950. Appreciation of members is due to Dr. H. H. Stewart, Dr. G. B. Maitland and Dr. Leigh Cook for the hard work and the time they expended on this schedule, and we take this opportunity of thanking them for their efforts in helping to bring this matter to a most satisfactory conclusion.

Post-Graduate Work.

During 1950 the Post-Graduate Committee, under the chairmanship of Dr. Ross Robinson, has had a most successful year. As usual the committee arranged all the scientific papers for the monthly British Medical Association meetings and assisted members in their post-graduate study by sponsoring visiting lecturers from overseas.

The most important feature of the post-graduate year was Post-Graduate Week, which was held in August, when the committee was fortunate in obtaining the services of Dr. Donald Hunter, of the London Hospital, and Professor Francis Blake, Dean of the School of Medicine at Yale, as visiting lecturers.

Dr. F. J. Browne, recently Professor of Obstetrics and Gynæcology at University College, London, lectured in Perth to members during May, and the committee was fortunate in being able to arrange for so prominent an obstetrician to visit the State.

Dr. Matthew Stewart, Professor of Pathology in the University of Leeds, has also recently lectured here, and during his short stay delivered two interesting lectures in Perth and one at Bunbury under the auspices of this committee.

Commencing on February 20 this year, the committee arranged a course of 24 lectures suitable for candidates for M.D. and M.R.A.C.P. examinations, and applications for the course far exceeded the expectations of the committee, which is most gratifying.

Publicity.

Following satisfactory negotiations to stamp out the threat of socialization of the profession, the Federal Council notified this Branch that it had recommended to the trustees of the Federal Independence Fund, and the trustees agreed, that the sum of money subscribed by members to reimburse the additional expenses occurred in publicity, in addition to the sum granted by the Federal Council, was being returned to the association for refund to its members. This has been done, the Independence Fund account being thereby closed.

Contract Practice Committee.

The Council is particularly appreciative of the untiring efforts of the contract practice committee on behalf of all members of the association. The committee's chairman, Dr. O. R. Corr, deserves special thanks in view of the time and attention he has given so willingly. The committee negotiated with complete success all agreements submitted for its consideration. The following are the rates of payment for contract practice during the year:

Lodge.—Full member: metropolitan, 50s.; country, 58s. Female: metropolitan, 38s.; country, 42s. Junior: metropolitan, 26s.; country, 28s.

Timber and Mining Agreement Fees.—Standard timber mill agreement, 58s. Special timber mill agreement, 80s. Mining agreement, 58s.

Special rates other than above are applicable to certain agreements where particular circumstances pertain.

Social.

There were three main social events during the year, the golf match held between the British Medical Association and the Law Society and two British Medical Association dinners.

The golf match was held at the Karrinyup Country Club and was followed by a dinner, during which several items were enjoyed by those present. The British Medical Association beat the Law Society this year, and in addition to a most satisfactory function both professions decided on this occasion that as this was an annual event and up until now members of both sides had had to subscribe, a fund be opened to be known as the Medico-Legal Golf Account, into which surplus money in excess of expenses should be paid, so that ultimately the match could be conducted with considerable reduction of cost to the participants. The fund stands at a credit of approximately £15.

The annual dinner of the association was held at the Ocean Beach Hotel, Cottesloe, on August 5, when Professor Blake and Dr. Donald Hunter were guests of honour, and about sixty members attended.

During the visit to Perth of Dr. John Hunter, General Secretary of the Federal Council, this Council entertained Dr. Hunter at dinner at the Esplanade Hotel. Dr. John Hunter also attended a special meeting of members on Sunday, June 18, when he addressed those present on all aspects of the conference during that month between the Federal Council and the Federal Minister for Health.

Staff.

The Council wishes to express to the office and library staff its sincere thanks for their cooperation and help to the association during the year.

INDUCTION OF PRESIDENT.

Dr. Aberdeen then took the chair as president, and Dr. J. Stubbe assumed the position of honorary secretary.

NEW SOUTH WALES BRANCH NEWS.

Medical Services to Subvention Members of Friendly Societies.

THE provision of medical services on a capitation basis to subvention members of friendly societies in New South Wales will cease on June 30, 1951. As from that date medical services will be rendered on a fee-for-service basis.

As the result of a recent amendment to the *Friendly Societies Act*, the State Government will pay the contributions of subvention members to the medical benefits schemes of the various friendly societies. Such contributions, however, will apply only in respect of general practitioner services.

The Act provides further that the medical funds may reimburse the member for the whole or part of the fees charged by the medical practitioner.

The Act provides also that the Government may refuse subvention to certain prescribed persons. Members entitled to the benefits of the Pensioner Medical Service of the Commonwealth Government may be so prescribed.

Correspondence.

DETECTION OF THE UNRECOGNIZED DIABETIC.

SIR: It was with great interest that I read your editorial in THE MEDICAL JOURNAL OF AUSTRALIA of May 26, 1951, connected with the organized drives conducted in America for the detection of unknown diabetics.

The Diabetic Association of Australia has been established with objectives similar to those of the English and American organizations. But, whereas they are mainly controlled and directed by medical men, the Australian committee is non-professional. A medical panel gives most valuable help and advice, but otherwise takes no part in its management.

Consequently your suggestion that the profession might assume greater responsibility in the detection of the unknown diabetic is most important.

The aim of our association is to cooperate with medical and public health authorities wherever possible, to help

diabetics by means of the journal and other activities, and to spread knowledge generally as to the diabetic "way of life".

Some small attempts have been made during Health Weeks to test for detection of unknown cases, but these have been purely experimental, and have merely proved that a properly organized and complete survey would provide valuable results. Such a survey could best be undertaken by some public health authority with the interested backing of the medical profession.

Our association would gladly cooperate in such a venture. In the meantime we hope to establish, as soon as possible, a permanent centre in the city. A small government subsidy, granted this year, has enabled us to find some office space and to instal a part-time secretary.

There is a Branch Association in Newcastle, but none in other States. I very much hope that the publicity given by your journal to this subject will arouse the active interest of people in other parts of Australia for this necessary community work.

Yours, etc.,

RUBY W. BOARD,
President, The Diabetic Association of Australia.

Box 4746,
G.P.O.,
Sydney.
June 6, 1951.

CONDITIONS OF ELIGIBILITY FOR COMMONWEALTH TUBERCULOSIS ALLOWANCE.

SIR: At the last meeting of the National Tuberculosis Advisory Council, Dr. Cotter Harvey said that some private practitioners were under the mistaken belief that a sufferer from tuberculosis, to be medically eligible for Commonwealth tuberculosis allowance, would need to be totally and permanently incapacitated by the disease. Dr. Harvey added that it would be helpful to the profession if the actual position could be made known through THE MEDICAL JOURNAL OF AUSTRALIA.

Total and permanent incapacity is definitely not a prerequisite to the granting of tuberculosis allowance. The object of the allowances scheme is to enable sufferers, both in their own interests and in the interests of the community at large, to undergo treatment immediately it is known that they are suffering from significant tuberculosis. The earlier the disease is detected the better, and tuberculosis allowance will be granted accordingly.

The full medical and disciplinary requirements of the allowances scheme are that the applicant (*a*) is suffering from tuberculosis, in whatever form, which has not been arrested; (*b*) should, in the opinion of the medical referee, refrain from working and take treatment; (*c*) is not working; (*d*) is undergoing treatment in an institution with which the medical referee is satisfied; (*e*) is undergoing domiciliary treatment (where that is desirable or where institutional accommodation is not available) under conditions satisfactory to the medical referee; (*f*) shall undergo such examination (including medical and radiological) as the medical referee may from time to time require; and (*g*) shall conduct himself or herself in a manner which, in the opinion of the medical referee, is in the best interests of the campaign against tuberculosis.

If you could give publicity to these matters in the journal, either by publishing this letter or in some other appropriate manner, I should be grateful.

Yours, etc.,

H. E. DOWNES,
Acting Director-General of Health.

Canberra,
June 8, 1951.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1945, as duly qualified medical practitioners:

Kettle, John Henry, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Kinny, Noel Wesley, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Kirkland, Thomas Hamilton Speirs, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

Knispel, Marie June, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Balmain.

Knox, Eleanor Charis, M.B., B.S., 1951 (Univ. Sydney), Rachel Forster Hospital, Redfern.

Korner, Paul Ivan, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Kosman, Edward, M.B., B.S., 1951 (Univ. Sydney), 24 Wentworth Avenue, Mascot.

Lake, Bernard Joel, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Lane, Margery Ritchie, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.

Latham, Geoffrey Rourke Welsford, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Balmain.

Learoyd, Harry Meldrum, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.

Lewis, Richard John Reynette, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Lewis, Ronald Gordon, M.B., B.S., 1951 (Univ. Sydney), 19 Boronia Road, Bellevue Hill.

Lucas, William Gerald, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

McDonald, Colin James, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

McFadden, John Brian, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

McGill, John Charles, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Marrickville.

McKinnon, Donald James, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

Madew, Lindsay Edward, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Marshall, Martin Hamilton, M.B., B.S., 1951 (Univ. Sydney), Prince Henry Hospital, Little Bay.

Masters, Floyd George, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Auburn.

Michell, George, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.

Middleton, Roland William Donald, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Mira, William John Dickson, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Mitchell, Robert Ian, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Mitchell, Robert Wentworth, M.B., B.S., 1951 (Univ. Sydney), Dubbo Base Hospital, Dubbo.

Monk, Marjorie, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Morgan, Noel John, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Wallsend.

Morrison, Dorothy Mary, M.B., B.S., 1951 (Univ. Sydney), St. George Hospital, Kogarah.

Morrissey, Matthew John, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.

Mulhearn, Richard John, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Myers, Geoffrey Stratford, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Lithgow.

Nelson, William Paul, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Orr, John Morgan, M.B., B.S., 1951 (Univ. Sydney), Western Suburbs Hospital, Croydon.

Orr, Kevin Bridson, M.B., B.S., 1951 (Univ. Sydney), Grafton Base Hospital, Grafton.

O'Sullivan, Brian Francis, M.B., B.S., 1951 (Univ. Sydney), Mater Misericordiæ Hospital, Crow's Nest.

Packard, Robert Spencer, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Papworth, Reginald Arthur, M.B., B.S., 1951 (Univ. Sydney), 7 Small Street, Willoughby.

Paton, Anthony Sutherland, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Hornsby.

Peisley, Hazel Norma, M.B., B.S., 1951 (Univ. Sydney), Orange Base Hospital, Orange.

Penna, Teresio, M.B., B.S., 1951 (Univ. Sydney), Wagga Base Hospital, Wagga.

Pennington, Arthur Frederick, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Parramatta.

Perry, Grace Amelia, M.B., B.S., 1951 (Univ. Sydney), St. George Hospital, Kogarah.

Pittar, Doreen Julie, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Pringle, Harry Mossman, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Goulburn.
Pullen, Peter David, M.B., B.S., 1951 (Univ. Sydney), Ryde District Hospital, Eastwood.
Reid, Bevan Leslie, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Rigg, Charles Andrew, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Rivett, Ronald Albert, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.
Robson, Alastair Geoffrey Grindrod, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.
Roche, John Vincent, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.
Rogers, James Stewart, M.B., B.S., 1951 (Univ. Sydney), Mater Misericordiæ Hospital, Crow's Nest.
Rooney, John Russell, M.B., B.S., 1951 (Univ. Sydney), Mater Misericordiæ Hospital, Crow's Nest.
Ryan, Anthony Ian, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Ryan, James Francis, M.B., B.S., 1951 (Univ. Sydney), Mater Misericordiæ Hospital, Waratah.
Scarlett, Geoffrey Anthony Gerard, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.
Schnitzler, George Julius, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.
Scrivener, Barrie Pedder, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Shapiro, Colleen Juanita Ann, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Bathurst.
Sharkey, Bryan Edmund, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Sharp, Andrew Cruickshanks Fallow, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Inverell.
Shearer, Charles Allan, M.B., B.S., 1951 (Univ. Sydney), Royal South Sydney Hospital, Zetland.
Shearman, Rodney Philip, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Sheehan, Anthony Hawthorne, M.B., B.S., 1951 (Univ. Sydney), Western Suburbs Hospital, Croydon.
Shellshear, Stuart Wilton, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Maitland.
Shiels, Eleanor Mary, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Short, Donald Wheeler, M.B., 1951 (Univ. Sydney), Temora and District Hospital, Temora.
Shumack, Ian Albert, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.
Skein, Marie Joyce, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Smithurst, Barry Anthony, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.
Soper, Henry Lewry, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Stackpool, Francis Michael, M.B., B.S., 1951 (Univ. Sydney), Brentwood Hospital, Muswellbrook.
Stehbens, William Ellis, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Stephens, Frederick Oscar, M.B., B.S., 1951 (Univ. Sydney), Royal South Sydney Hospital, Zetland.
Stephenson, John Hunter, M.B., B.S., 1951 (Univ. Sydney), Ryde District Hospital, Eastwood.
Sullivan, Neville Nelson, M.B., B.S., 1951 (Univ. Sydney), St. George Hospital, Kogarah.
Swenson, Patricia, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.
Tellesson, Thomas Keith, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Hornsby.
Tellesson, William George, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.
Thornton, Sydney Melford, M.B., B.S., 1951 (Univ. Sydney), Wagga Base Hospital, Wagga.
Tomkins, John Anton, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Tonkin, John Paul, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.
Turner, Brian Baxter, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Tweedale, Kenneth, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 2, 1951.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Ankylostomiasis	*	..	..	..	..	..	..	..	..
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	..	2(1)	2(1)	2	..	..	..	1	7
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	5(5)	..	..	..	..	..	5
Diphtheria	14(4)	6(2)	3(3)	1(1)	5(4)	..	..	..	29
Dysentery (Amœbic)	*	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	*	3(3)	13(13)	..	5(5)	..	..	..	21
Encephalitis Lethargica	..	..	..	..	..	..	..	..	..
Erysipelas	*	*	*	..	*	*	..	..	..
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	..	*	*	..	*	*	..	..
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	..	*	*	*	*	*	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	*	..	..	..	..	..	..	..	..
Measles	*	*	*	46(4)	*	*	..	..	46
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	35(19)	4(3)	25(7)	23(17)	1(1)	..	..	..	88
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	1	..	..	..	..	..	1
Rubella(*c*)	*	*	..	*	6	*	..	..	6
Scarlet Fever	9(4)	26(12)	3	6(2)	5(5)	2(1)	..	..	51
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	..	..	*	*	*	*	..
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(*d*)	19(16)	9(6)	29(23)	8(5)	11(7)	4(1)	..	..	80
Typhoid Fever(*e*)	..	1(1)	..	..	1	..	..	..	2
Typhus (Endemic)(*f*)	4(1)	..	.	..	1(1)	..	..	..	5
Undulant Fever	..	..	..	..	..	..	..	..	..
Weil's Disease(*g*)	*	*	..	*	*	*	*	*	..
Whooping Cough	*	*	*	..	*	*	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from the Northern Territory.
* Not notifiable.
(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Twist, Elaine Mary, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.
Vickery, Ronald Burgess, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Marrickville.
Voss, John Henry Edward, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.

Obituary.

CHARLES HENRY CORMAC.

WE regret to announce the death of Dr. Charles Henry Cormac, which occurred on June 13, 1951, at Wynnum Central, Queensland.

Congresses.

INTERNATIONAL CONGRESS OF CLINICAL PATHOLOGY.

THE International Congress of Clinical Pathology will be held in London from July 16 to 20, 1951. All those interested are invited to attend. Inquiries should be addressed to the Secretary-Treasurer, Dr. W. H. McMenemey, Maida Vale Hospital for Nervous Diseases, London, W.9.

Nominations and Elections.

THE undermentioned have been elected members of the New South Wales Branch of the British Medical Association:

Ackary, John Francis, M.B., B.S., 1951 (Univ. Sydney), St. George Hospital, Kogarah.
Cook, Samuel West, M.B., B.S., 1951 (Univ. Sydney), 21 Alexandra Street, Hunters Hill.
Croucher, Colin, M.B., B.S., 1950 (Univ. Adelaide), 105 Sulphide Street, Broken Hill.
Deakin, Malcolm James, M.B., B.S., 1951 (Univ. Sydney), R.A.A.M.C., B.C.O.F., Japan.
Dobell-Brown, David Leslie, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.
Fisher, Adrian Welby, M.B., B.S., 1951 (Univ. Sydney), Armidale and New England Hospital, Armidale.
Gerdes, William Thomas, M.B., B.S., 1945 (Univ. Sydney), 7 Moore Street, Austinmer.
Goodman, Harry Thomas, M.B., B.S., 1950 (Univ. Sydney), Haylock Street, Tullamore.
Halloran, Audrey, M.B., B.S., 1951 (Univ. Sydney), St. George Hospital, Kogarah.
James, George Robert, M.B., B.S., 1951 (Univ. Sydney), 24 Banks Street, Brighton-le-Sands.
Knispel, Marie June, M.B., B.S., 1951 (Univ. Sydney), Balmain and District Hospital, Balmain.
Korner, Paul Ivan, M.B., B.S., 1951 (Univ. Sydney), 3 Hunter Street, Woolwich.
Larum, Cornelius Lloyd, M.B., B.S., 1950 (Univ. Sydney), St. Joseph's Hospital, Auburn.
Lester, Vincent, registered in accordance with the provisions of Section 17 (1) (c) of the *Medical Practitioners Act*, 1938-1945, 10 Kingston, 17 Harriette Street, Neutral Bay.
Lindsell, Charles Kenneth, M.B., B.S., 1950 (Univ. Sydney), 153 Fullers Road, Chatswood.
Mayne, Robert John Bruce, M.B., B.S., 1951 (Univ. Sydney), 22 Bent Street, Lindfield.
McKenzie, Nancy, M.B., B.S., 1950 (Univ. Sydney), Broken Hill and District Hospital, Broken Hill.
Reid, Stanley Edward, M.B., B.S., 1950 (Univ. Melbourne), Manly District Hospital, Manly.
Smithurst, Barry Anthony, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.
Spencer, Terence Edward Thornton, M.B., B.S., 1951 (Univ. Sydney), Moorabinda, Tenterfield.
Tidswell, Thomas, M.B., B.S., 1951 (Univ. Sydney), Berrima District Hospital, Bowral.
Vickery, Ronald Burgess, M.B., B.S., 1951 (Univ. Sydney), Marrickville District Hospital, Marrickville.
Watson, Lyal Clifton Albert, M.B., B.S., 1950 (Univ. Sydney), 20 Tryon Road, Lindfield.

Medical Appointments.

Dr. Vernon Douglas Plueckhahn has been appointed clinical research officer to the Council of the Institute of Medical and Veterinary Science, Adelaide.

Dr. Brian Joseph Shea has been appointed resident medical officer for mental institutions in the Hospitals Department, Adelaide.

Dr. Esmond Frank West has been appointed to the Physiotherapists Board of South Australia.

Diary for the Month.

JULY 3.—New South Wales Branch, B.M.A.: Council Quarterly.
JULY 4.—Victorian Branch, B.M.A.: Branch Meeting.
JULY 4.—Western Australian Branch, B.M.A.: Council Meeting.
JULY 5.—South Australian Branch, B.M.A.: Council Meeting.
JULY 6.—Queensland Branch, B.M.A.: Branch Meeting.
JULY 6.—Tasmanian Branch, B.M.A.: Council Meeting.
JULY 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee. Organization and Science Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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